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ACUTE CHOLECYSTITIS

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BOSTON

A DIFFERENCE of opinion exists today in regard to the treatment of acute cholecystitis. Until a few years ago there was general agreement that a policy of delaying operation until the acute signs and symptoms of the disease had subsided gave the best results. But in recent years the question has been raised as to whether the traditional conservative policy of delay is actually safest and most satisfactory,[1] or whether acute cholecystitis should, like acute appendicitis, be treated with immediate or early operation.

Shortly after this argument began, the cases of acute cholecystitis treated in the Peter Bent Brigham Hospital over a period of twenty years were reviewed to determine the results obtained. It was found that there was no consistent lowering of the mortality rate, which was 10.7 per cent for the 235 cases treated surgically.[2] This mortality rate seemed too high, and not in keeping with the general improvement in the care of surgical patients during this period. Accordingly it was decided to vary from the uniform standard policy of delay to determine if possible in each case just when surgery was advisable, whether this appeared to be within a few hours of admission to the hospital in fulminating cases or after several days of conservative treatment.

Since that time each patient entering the hospital has been treated as an individual surgical problem after the following plan of treatment. Once the diagnosis of acute cholecystitis is made, immediate hospitalization is urged, regardless of how slight the signs and symptoms may be. This cannot be accomplished unless the family physician considers the diagnosis of acute cholecystitis, like that of acute appendicitis, mandatory for hospitalization. Hospitalization does not necessarily mean that immediate surgery will be carried out, but merely that general measures will be instituted in preparation for surgery at a favorable time. On admission to the hospital, immediate measures are taken to relieve pain and to establish fluid balance by the intravenous route, the routine laboratory work is done and the extent and severity of the inflammatory process involving the gall bladder are estimated. Signs, symptoms and laboratory data are evaluated frequently. In severe cases, such determinations are made at night as well as during the day. Whether or not early operation is performed depends on the progress of the inflammatory process after such therapy has been instituted. Early operation is carried out if the inflammatory process in the right upper quadrant progresses, or if there are signs of general peritoneal irritation. Stereotyped management in the treatment of acute cholecystitis is unsatisfactory, because each patient is an individual surgical problem, and because the optimum time for operation varies with each case.

An analysis was made of 121 consecutive cases of acute cholecystitis treated by operation in the Peter Bent Brigham Hospital during the last five years to determine the patients' clinical response following the above outlined plan of treatment (Fig. 1). Approximately one fourth of the patients entered the hospital either after the acute attack had subsided or in the terminal stages of an acute attack, Group A. A second group, B, slightly smaller, responded promptly to treatment, with a return of the temperature, white-cell count and physical findings to normal within forty-eight hours. This is the type of response that the clinician usually expects, but unfortunately one that does not always occur. About as many patients fell into Group C and had an exacerbation of symptoms after forty-eight hours of conservative treatment as were in Group B, which responded early. Since a clinician cannot foretell which patient will get worse under conservative treatment, this is a strong argument in favor of early hospitalization. The greatest number of patients fell into Group D and required more than three days for the temperature to subside and the signs of inflammation to abate. A few cases, less than 10

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per cent, remained stationary, that is, the temperature, white-cell count and physical findings did not respond to conservative treatment in Group E. In such cases the clinician should be suspicious of acute suppurative cholecystitis, possibly with a localized extracholecystic abscess. The patients

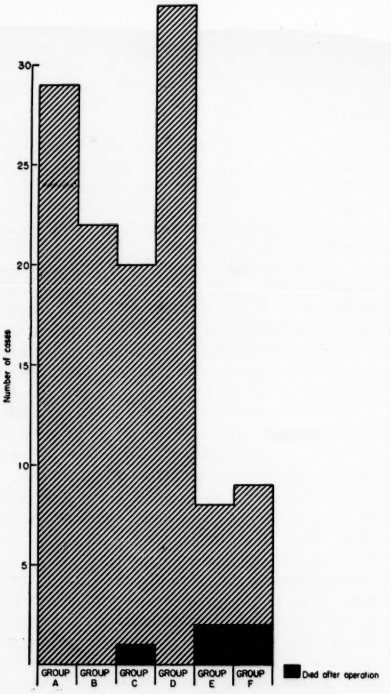

FIGURE 1. *Clinical Response to Hospitalization.*

Group A: *acute signs and symptoms already subsided by time of admission;* Group B: *acute signs and symptoms promptly subsided in forty-eight hours;* Group C: *early improvement for forty-eight hours, followed by exacerbation of signs and symptoms;* Group D: *acute signs and symptoms persisted three days or longer;* Group E: *acute signs and symptoms persisted without response to conservative treatment;* Group F: *acute signs and symptoms increased in severity under conservative treatment.*

making up Group F presented a fulminating type of infection, with rapid progress of the disease, probably owing to an overwhelming infection. The mechanical and chemical factors do not play an important role in this group. Four of the five deaths occurred in the last two groups, made up largely of the severe cases. It is apparent that not all cases of acute cholecystitis subside even under ideal treatment. The surgeon, therefore, must observe these patients with acute cholecystitis early and frequently to decide in each case the most suitable time for operation.

Although immediate hospitalization is urged once the diagnosis of acute cholecystitis has been made, regardless of how slight the symptoms may

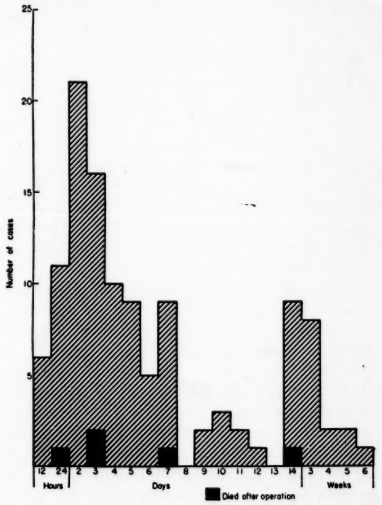

FIGURE 2. *Duration of Acute Symptoms before Hospital Admission.*

appear to be, as a matter of fact only about one third of the 121 patients in this series were sent to the hospital promptly, so that in the majority of cases, even if it had been desired, operation within forty-eight hours of the onset of the acute attack would have been impossible (Fig. 2). In only 3 cases during the five-year period did it seem advisable to operate on the patient within twelve hours of the time of admission to the hospital (Fig 3). These patients were very ill, and the possibility of a perforated viscus could not be ruled out. In 12 cases operation was performed from twelve to twenty-four hours after admission; in 16, on the second hospital day. In other words, 25 per cent of the patients in the series were operated on within forty-eight hours of admission to the hospital. The remaining 75 per cent were hospitalized seventy-two or more hours before opera-

tion. These figures refer to the period of hospitalization only and bear no relation to the duration of acute symptoms. This important factor, the length of time elapsing from the onset of acute symptoms until operation, is shown graphically in Figure 4. Despite the fact that 25 per cent of the patients were operated on within forty-eight hours of admission, on the basis of time elapsing from the onset of acute symptoms until operation this figure is reduced to 7 per cent. The clinician who first sees the patient must urge hospitalization promptly, so that the surgeon may choose the most suitable time for operation.

The incidence and dangers of perforation have contributed to the differences of opinion in the treatment of acute cholecystitis, for it is recognized

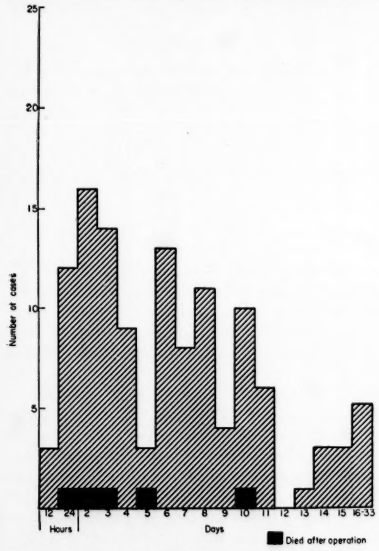

FIGURE 3. *Days of Hospitalization before Operation.*

that, in general, perforation increases the mortality and that at times the clinician cannot tell which case may result in a perforation of the gall bladder.[8] As a rule, persistent pain and an increasing leukocytosis with increasing local signs of inflammation or persistent symptomatology under treatment imply that the gall bladder has perforated. However, physical findings and laboratory data do not always give reliable information as to the extent of the pathologic process involving the gall bladder, and for this reason early hospitalization and frequent evaluation of the patient's progress are imperative to maintain a low mortality. Except in rare cases, the perforation is walled off by the omentum and adjacent tissue, making an extracholecystic abscess. Perforation occurred in 16, or 13 per cent, of the 121 cases under discussion,

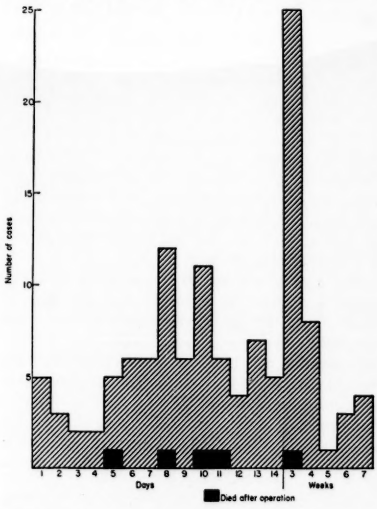

FIGURE 4. *Duration of Acute Symptoms from Onset until Operation.*

with a mortality of 6 per cent (Table 1). In all but one case, a walled-off abscess resulted. The perforation is rarely free in the peritoneal cavity.

TABLE 1. *Incidence of Perforation.*

Pathologic Lesion	No. of Cases	Average Duration of Acute Symptoms before Hospitalization
		days
Abscess about fundus	5	7
Abscess about ampulla	4	8
Abscess into liver	4	4
Perforation into intestine	2	2
Free perforation	1	1
Total	16*	

*Seven patients had no previous biliary symptoms.

However, there was one case with a free perforation, wherein the omentum was attached to the site of a gastric resection, performed years before.

Postoperative complications were present in 25 patients, approximately 20 per cent of the entire group (Table 2). As would be expected in upper abdominal surgery, a large percentage of these were pulmonary complications, such as atelectasis, with

complications as the result of infection the second most frequent. Each case was evaluated carefully, and any deviation from the normal course, regardless of how slight, was regarded as a complication.

Infection and pulmonary embolus were the chief causes of death (Table 3). In addition to acute

TABLE 2. *Complications.*

COMPLICATION	NO. OF CASES
Pulmonary	13
Wound infection	6
Miscellaneous	6
Total	25

cholecystitis, there was in each case a second serious complication—a calculus located outside the gall bladder. A stone was either in the common or hepatic duct, or else had eroded through the gall bladder into the intestine.

The ages of the patients were fairly well distributed, so that the mortality was not high in those above the age of sixty-five; in fact there was only one death in the 21 patients over sixty-five years of age (Fig. 5). We believe that advanced age in itself does not contraindicate surgery in acute cholecystitis.[4]

By treating the patient with acute cholecystitis as an individual surgical problem and by depend-

TABLE 3. *Causes of Death.*

AGE yr.	OPERATION	FINDINGS AT OPERATION	CAUSE OF DEATH
48	Cholecystostomy	Acute cholecystitis	Abscess of liver (calculi in hepatic duct)*
63	Cholecystostomy	Acute cholecystitis and acute pancreatitis	Peritonitis and multiple abscesses (gallstone in duodenum)*
71	(1) Cholecystostomy (2) Cholecystectomy and choledochostomy	Acute cholecystitis Chronic cholecystitis, common-duct stone and acute pancreatitis	Peritonitis and cardiac failure
59	Cholecystectomy and choledochostomy	Acute cholecystitis and common-duct stone	Pulmonary embolus*
63	Partial cholecystectomy and closure of cholecystoduodenal fistula	Subacute cholecystitis	Pulmonary embolus (gallstone in ileum)*

*Verified by autopsy.

ing on the response to hospitalization to determine the optimum time for surgery, either early or late, we have been able to reduce the mortality rate during the last five years from the former percentage of 10.7 to 3.8, a difference of 6.9 per cent, which is more than twice its standard error and therefore of statistical importance (Table 4). The gall bladder was removed in 71 cases, with a mortality rate of a little over 1 per cent, which is only a fraction higher than that for chronic cholecystitis. In 40 cases, choledochostomy was combined with cholecystectomy, with a mortality rate of 5 per cent. It is most important for the surgeon to remember that common-duct stones occur in association with acute cholecystitis, for many clinicians believe that a stone blocking the cystic duct more or less certifies the absence of a common-duct stone.

TABLE 4. *Surgical Treatment.*

OPERATION	NO.	MORTALITY %
Cholecystectomy	71	1
Cholecystectomy and choledochostomy	40	5
Cholecystostomy*	18	11
Cholecystostomy and choledochostomy	2	–
Total	131	3.8

*Ten patients had subsequent operations.

We have found common-duct stones in 20 cases of acute cholecystitis, an incidence of 15 per cent, which is almost as high as that in the cases of

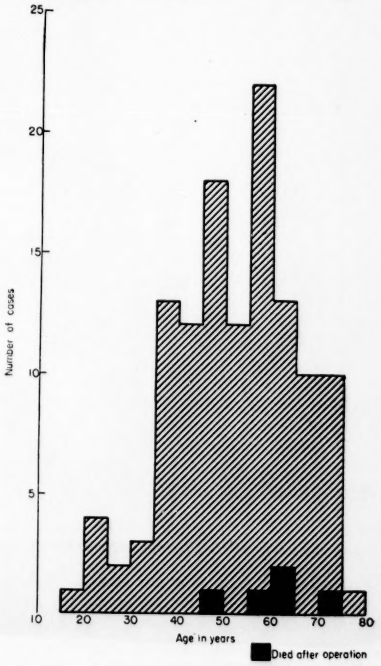

FIGURE 5. *Age Distribution.*

chronic inflammation. From the literature, it appears that the surgeons performing early operation routinely do not find so many common-duct stones.[5] The high mortality associated with a second operation for exploring the common duct to remove the overlooked stone will in the long run, I believe, counterbalance the initial low mor-

tality. The mortality rate for cholecystostomy was high (11 per cent), but this procedure was carried out in only the severest cases. Cholecystostomy is a valuable method, and the surgeon should not hesitate to utilize it when he doubts the safety of cholecystectomy.[6] Except in patients who are very poor risks, cholecystectomy follows cholecystostomy, either in the same period of hospitalization or within a few months.

Improvements in the general care of surgical patients, such as attention to fluid balance, must receive due credit for reducing postoperative mortality in recent years. However, individualization of the treatment of the patient with acute cholecystitis has played a considerable role in this lowered mortality and is perhaps more important than a strict adherence to a standard policy of treatment.

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Summary

Immediate hospitalization should follow the diagnosis of acute cholecystitis.

Each patient with acute cholecystitis is an individual surgical problem. The optimum time for operation depends on the patient's response to preoperative treatment.

A mortality rate of 3.8 per cent was obtained over a period of five years in the surgical treatment of 121 cases of acute cholecystitis.

A common-duct stone is a frequent complication of acute cholecystitis, and occurred in 15 per cent of our cases.

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THE CAUSES OF INDIGESTION AND THEIR RECOGNITION*

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PHILADELPHIA

THE words "indigestion" and "dyspepsia" suggest some disturbance in the chemical processes that food materials undergo in the gastrointestinal tract. That, of course, was the original explanation for the symptoms that so frequently develop in relation to the intake of food, and it is still the explanation given by most of the laity. Although it is now recognized that such chemical changes are of relatively minor importance, no more satisfactory term has been devised to indicate a syndrome that includes a subjective sensation of epigastric discomfort or pain, often related to meals, anorexia, gaseous eructations, regurgitations, nausea and vomiting, and sometimes headache, palpitations and general nervousness and weakness. For lack of a better term, I shall therefore refer to this group of symptoms, which is obviously related to the stomach, as "indigestion."

The justification for recognizing the syndrome is not that it constitutes a diagnosis, for after all it is no more a diagnosis than hypertension, dyspnea or jaundice is. But just as each of those terms connotes a group of clinical phenomena, explainable on the basis of a disturbed function of the body, so indigestion designates a picture of disturbed gastric physiology. The dysfunction is itself a manifestation of some more fundamental disorder of the body; the identification of that disorder constitutes the diagnosis.

Irrespective of the diagnosis, the clinical manifestations of indigestion are probably always immediately dependent on a disturbance of the motor function of the stomach, rarely of the secretory function. Distress or pain in the epigastrium is believed to be due to an increase in the tension of the stomach walls, which in turn may be incident to spasm, especially of the cardia, pylorus or proximal duodenum, to increased tone of its general musculature, to overfilling of the organ or to variations in the normal progression of its peristaltic waves. Eructations, regurgitations, nausea and vomiting, even anorexia, are also believed to be the result of a motor disturbance of some kind, at times to an actual reversal of the peristaltic waves. Thus though indigestion may have many and varied causes, it apparently always in itself represents a localized motor disturbance of the stomach. Secretory alterations are today believed to be important chiefly because of their effects on the motor function of the stomach.

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In searching for the ultimate causes of indigestion one must therefore consider the mechanisms that control the motor functions of the stomach. Like other muscular structures, its walls normally possess a certain degree of tonicity or of contractility, this phenomenon being, in part, intrinsic and, in part, dependent on the innervation of the organ by the autonomic nervous system. The same autonomic nerves that supply the gastric muscles also supply other parts of the digestive tract, the liver and the gall bladder, the pancreas and the genitourinary organs. This relation undoubtedly accounts for so-called "reflex disturbances" in the stomach secondary to disease in those organs. Also, since the autonomic nervous system has a center in the hypothalamus, one can understand how certain cerebral organic lesions, even emotional disturbances, may set up alterations in the functions of the stomach. One thinks of the vomiting in massive brain lesions, of the nausea and vomiting in seasickness and migraine, of the gagging that occurs in some people on viewing a revolting scene, of the aerophagia, belching, nausea and vomiting that not infrequently develop under great emotional strain, as in the presence of a serious accident or the death of a relative. I need not pursue the illustrations, except to point out that vague digestive disturbances often originate in prolonged and less critical emotional stress, as in domestic quarrels, business upsets and undue mental fatigue.

The motor functions of the stomach may also be disturbed as a result of the local circulatory alterations that occur in cardiac decompensation or from portal obstruction. Indigestion is often the first manifestation of a failing circulation, of cirrhosis of the liver or of portal thrombosis. It may, likewise, result from toxic substances, acting locally or on the central nervous system, as in uremia, drug poisonings and certain general infections, such as typhoid fever, pneumonia and especially scarlet fever and other childhood infections.

Finally, disturbed motor function occurs as a result of local gastric lesions: gastritis, ulcer, tumors, pressure from the outside or intrinsic cicatrices. These may act directly by producing spasm of the gastric musculature or organic obstruction, interfering with either the normal entrance or exit of the gastric contents.

It is customary to speak of the gastric dysfunction due to psychic or emotional disturbance as "nervous indigestion," a gastric neurosis or functional dyspepsia; as a matter of fact, however, relatively few cases of indigestion are caused by organic disease of the stomach, and it is equally fitting to regard the indigestion of appendicitis, of gall-bladder disease or of an organic brain or spinal-cord lesion as functional. Even the indigestion of carcinoma or ulcer of the stomach is mainly the result of associated functional abnormalities of the stomach, superimposed on some locally irritating or obstructive phenomenon. In all cases, therefore, one may think of indigestion as a functional disturbance — a local motor dysfunction of the stomach resulting from faulty impulses reaching it through the nervous system, from toxins reaching it through the mouth or through the blood stream or from some locally acting factor, such as congestion, overfilling of the lumen of the organ or the presence of an irritating or mechanically obstructive lesion.

In spite of this viewpoint regarding the mechanism of indigestion and in deference to custom, we have continued, in our gastrointestinal clinic, to group under the heading of "functional gastric disturbance" or "gastric neurosis," all cases that cannot be explained as the result of an organic disease of the gastrointestinal tract or its associated organs. Our analysis (Fig. 1) is based on

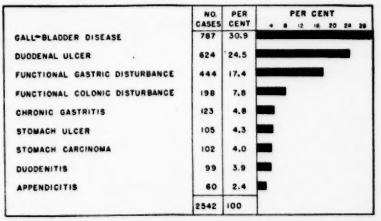

FIGURE 1. *Incidence of the Commoner Gastrointestinal Lesions that Produce "Indigestion."*

2542 cases of indigestion, 17 per cent of which were found to be functional. It is to be remembered that in such a clinic the cases are selected; those with obvious cerebral lesions, cardiovascular or renal disease and general infections go elsewhere in the hospital. The functional group, therefore, consists largely of patients whose symptoms are nonorganic. In private practice the functional group, even on such a basis of classification, is, of course, much larger — usually over 50 per cent.

Most of the 17 per cent have resulted from psychic or emotional disturbance, from anxiety states, fears, domestic turmoil and maladjustments in general. They are sent by general practitioners, who often suspect the nature of the trouble but consider it important to eliminate organic disease. Surprisingly, the mere demonstration of the absence of such disease alone cures many patients. With others, when the facts can be secured and the situation rationalized, the symptoms disappear.

With still others, help must be sought from mental hygienists, but this number is small. One wonders if even psychiatrists realize how many of these cases are satisfactorily handled by the resourceful and intelligent family physician or internist.

I shall now consider those patients who developed the syndrome on the basis of organic disease in the gastrointestinal tract or its associated organs.

Figure 1 shows that the largest number, 31 per cent, of the patients were proved eventually to have gall-bladder disease, with or without stone. This observation is of great importance because it suggests that the gall bladder should always be suspected in every case of indigestion and eliminated before other causes are seriously considered. A probable diagnosis of cholelithiasis can often be made on the basis of a characteristic history of biliary colic, especially when associated with local tenderness or jaundice, but often, even in the presence of stone, and commonly, when no stone is present, the symptoms are similar to those of any other type of gastric dysfunction, consisting chiefly of vague discomfort, eructations, regurgitations, sometimes nausea and even vomiting. In such cases one should not eliminate the possibility of gall-bladder disease without obtaining both a biliary-drainage test and a cholecystogram. Sometimes one and sometimes the other may be negative, even in the presence of stone, but rarely will both tests give a negative result. Our experience with proved cases shows that by the use of one or the other test some abnormality may be demonstrated in more than 95 per cent and in an almost equal percentage of the cases without stones.

Duodenal ulcer is the next most frequent cause of indigestion — 24 per cent in our series. Its diagnosis or elimination on the basis of the patient's history is more accurately determined, but even in dealing with ulcer one should never trust the history alone, no matter how clearly the pain is related to the intake of food, how clear-cut its relief by alkalies or what the general course of the disease. An exactly similar picture may be present in the absence of ulcer. Gastric analysis is of relatively little help, although the acid figures in duodenal ulcer are usually high. X-ray study is of maximal importance. The accuracy of the roentgen-ray investigation in the diagnosis of ulcer, in good hands, is today probably 95 per cent, and in all questionable cases it should be employed.

The functional disturbances of the stomach come next in frequency, after gall-bladder disease and duodenal ulcer, and have been considered.

The group to which I refer in Figure 1 as "functional colonic disturbance" requires some explanation. This applies to functional disturbances of the stomach (indigestion) caused by some abnormality primary in the terminal ileum or colon; the latter may be organic or functional. It thus includes indigestion dependent on constipation, irritable colon, colonic diarrheas as well as terminal ileitis, diverticulitis and tumors of the colon. Perhaps I should also include cases of appendicitis, which, in spite of their general frequency, are rare in a medical clinic. In any event, all these disturbances that lead to stasis in the colon and terminal ileum, whether by spasm or organic obstruction, often produce a delay in gastric evacuation, with eructations, regurgitations, nausea and frequently vomiting. Intubation studies have clearly shown the influence of the spastic terminal ileum on gastric motility. This disturbance in the motility of the stomach may be reflex from below through the autonomic nervous system, or it may result from some more inherent nervous or muscular mechanism. At the moment I am concerned with the mere fact of its occurrence and with its contribution to the etiology of indigestion.

Bowel disturbances must not, therefore, be forgotten in searching for the cause of indigestion. They are to be found by a careful consideration of the history of the case, by physical examination, especially by digital examination of the rectum, by proctoscopy and by the barium enema. Many cases have gone unexplained for a long time because of failure to remember this possibility and to employ the proper diagnostic procedures.

Each of the organic diseases of the stomach itself — ulcer, carcinoma and gastritis — occurred in about 4 per cent of our total group. The diagnosis of gastric ulcer depends on the same clinical and laboratory data as that of duodenal ulcer. Gastric cancer, however, deserves special mention. It may give rise to only the vaguest symptoms, or to none, until all hope of cure has passed. Its early recognition, therefore, is so important that no case of indigestion — no matter how trivial and especially if it occurs in a person of middle age or beyond in whom the symptoms have developed without obvious cause — should fail to have adequate study. This should include gastric analysis, roentgenologic investigation and sometimes gastroscopy. The gastric analysis alone should never be relied on, since in our experience 20 per cent of the cases showed a normal or high free-acid content. The roentgen study, however, is of great importance and usually reveals the nature of the lesion, or at least indicates the need for further close observation. In the uncertain cases, the gastroscope may be of the greatest help, this type constituting one of the chief indications for its use.

Chronic gastritis is of equal frequency with ulcer and carcinoma of the stomach. Gastroscopy is definitely indicated when gall-bladder disease, ulcer and cancer have been eliminated and no probable explanation for the indigestion exists, even when the roentgen-ray study is negative. The time has passed for diagnosing gastritis on the basis of an alcoholic history, achlorhydria and mucus in the gastric contents. None of these may be present, and yet a well-developed atrophic or hypertrophic gastritis, curable by intelligent therapy, may be demonstrable. Whether or not atrophic gastritis is the cause of carcinoma of the stomach or pernicious anemia, it frequently precedes the development of those diseases; its recognition is important, therefore, if only to keep the subject under observation for the development of the signs of one of those more serious diseases.

I have placed little emphasis on the type of indigestion, which I believe has been overstressed in the past and is overstressed in modern textbooks. One hears too much about the gaseous eructations and night pains of gall-bladder disease, the relation of food to pain in ulcer, the boring pain of cancer of the stomach. These are helpful items of history, but often they are misleading and should not be allowed to determine the final working diagnosis in any case. The observations on physical examinations are rarely of significance in this type of disease; when positive, however, they may be of great assistance. Mistakes on the basis of the history and the physical examination alone are too costly; roentgen-ray investigation, biliary drainage, proctoscopic and gastroscopic studies, in spite of their trouble and expense, are timesaving and cheaper in the end for the patient and the doctor. The results must, however, be interpreted by the physician in correlation with his other clinical observations.

Summary

I have defined "indigestion" as a syndrome resulting from motor dysfunctions of the stomach, and have referred to its association not only with diseases of the stomach and intestines and their appendages, but also with various circulatory, toxic, psychic and emotional disturbances. I have also outlined the relative incidence of its commoner causes as encountered in the gastrointestinal clinic of a general hospital, and have emphasized the importance of a complete investigation of every patient with the syndrome, employing, in addition to a careful history and a thorough physical examination, all the available special diagnostic procedures.

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AN UNUSUAL CASE OF SUBDURAL HEMATOMA*

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IT HAS been an observation of increasing frequency that hematomas of the cerebral group, particularly subdural hematomas, may assume the characteristics of almost any cerebral lesion. Much has been written concerning post-mortem findings in such cases, and it is indeed no rarity for the neurosurgeon to operate on a supposed brain tumor, only to discover a subdural hematoma. Furthermore, it is now a well-established fact that operative exploration is the one method of ruling out the possibility of subdural hematoma in suspected cases.

In a series of 57 cases of cerebral hematoma, analysis has shown that in the great majority the preoperative diagnosis has offered no unusual difficulty. There was, however, one exceptional case in this group, and owing to its decidedly unusual character, it has been considered worth while to present it in the form of a report.

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CASE REPORT

A 38-year-old man was admitted to the Worcester City Hospital on June 3, 1933, with the complaint of headaches and a swelling of the right eye of 5 days' duration. X-ray examination confirmed the impression of severe pansinusitis. Shortly after admission, a turbinectomy was performed, together with drainage of an orbital abscess. After a hospital stay of 47 days, the patient was finally discharged improved with a diagnosis of pansinusitis.

FIGURE 1. *Encephalogram.*

The posteroanterior view reveals air over the left cortex, with the cortical markings present. There is little evidence of air over the right cortical surface. There is no shift of ventricular system from the mid-line.

The second admission occurred on August 28, 1933. During the interval of 2 months between admissions, the former symptoms returned. The patient complained of severe headaches and a low-grade afternoon fever. For the first time he also noted cloudiness of vision in the right eye. Routine examination showed an edematous and slightly reddened area about the right orbit, with tenderness to palpation. There was some exophthalmos. There was blurring of the right disk. Lumbar puncture revealed a pressure of 280 mm. of water. Subsequently, operation was performed, and the patient was found to have, in addition to the right frontal sinusitis, a right orbital abscess and an abscess involving the right frontal lobe of the brain. He was finally discharged free of symptoms on the 78th hospital day.

The patient was admitted on February 19, 1940, for the

FIGURE 2. *Encephalogram.*

The left anterolateral view, taken with forehead up, reveals evidence of air over the left cortex.

FIGURE 3. *Encephalogram.*

The right lateral view, taken postoperatively, reveals the extent of the field exposed at operation.

third time. He stated that during the interval of 7 years he had been perfectly well until approximately 2 weeks previous to admission. The diet had been adequate, and alcohol had been used sparingly. There had been no history of trauma of any kind. The present illness was ushered in by a head cold associated with headache. On the day before admission, except for these complaints, the patient appeared well; soon after retiring that evening, however, he became very restless, and it was noted that his face twitched slightly on the left side. Gradually, he became stuporous and was sent to the hospital. In the emergency ward he experienced 3 successive violent Jacksonian seizures involving the left side. These attacks were characterized by beginning twitching of the left side of the face, rapidly spreading into the left arm and then into the left leg. The seizures tended to subside in the reverse order of progression. Cyanosis and dyspnea were marked with each spell. Physical examination showed a slightly dilated right pupil and beginning edema of the right optic disk. The peripheral reflexes of the left side were increased over those of the right. On the left there were positive Babinski and Hoffmann reactions. There was some left-sided ataxia. Lumbar puncture was performed, and the initial pressure was found to be 210 mm. The total protein content was 22 mg. per 100 cc., with clear fluid. X-ray examination of the skull revealed nothing unusual except the old operative defect of the right frontal sinus. Following the lumbar puncture, moderate limitation of fluids and medication, the attacks became less frequent and severe during the next few days. However, they recurred suddenly and approached the condition of status epilepticus. The spinal-fluid pressure had risen to 260 mm., and the total protein to 40 mg. The diagnoses varied considerably, including brain tumor, recurring brain abscess and adhesive

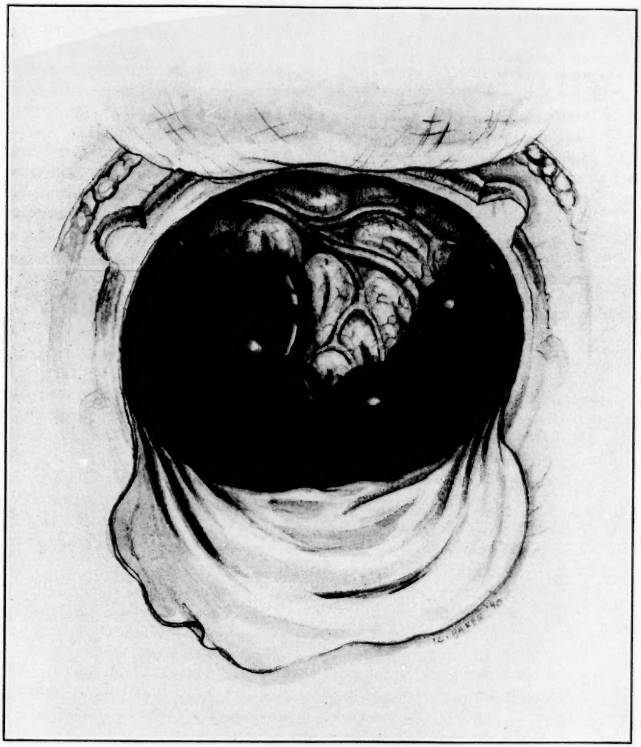

FIGURE 4.

This drawing shows the operative field through a right temporoparietal bone flap, with the subdural hematoma in situ. The lower portion of the clot has been removed, exposing the cerebral cortex.

arachnoiditis, with a question of cortical scarring. An air injection was performed to substantiate or to rule out an expanding lesion. The air films revealed no shift of the ventricular system. In the anteroposterior view, cortical markings were present on the left side, but on the right no air was visualized in the subarachnoid space. In other words, the x-ray films supported the diagnosis of chronic adhesive arachnoiditis, with cortical scarring involving the right side of the brain (Figs. 1 and 2).

A right-sided bone flap was turned down, and directly beneath the dura a large localized clot, approximately 2 cm. thick, was exposed (Fig. 3). The brain cortex directly underneath this clot was flattened and depressed. The arachnoid, when exposed after removal of the clot, was slightly thickened but not adherent, and did not have the gross appearance of chronic adhesive arachnoiditis (Fig. 4). Furthermore, no evidence of cortical scarring was noted on gross examination. The diagnosis was subdural hematoma.

The postoperative course was uneventful. The condition of status epilepticus was completely relieved, and the patient experienced no further seizures. He was finally discharged on the 17th postoperative day, without complications. Since discharge, the patient has been followed at regular intervals. The abnormal neurologic findings gradually disappeared. He has been working at his old job in a machine shop and has experienced no ill effects. His general condition at the present time is described in his own words as "never felt better."

This case raises several interesting points. The first is whether or not the underlying brain involvement due to abscess formation resulted in any delayed contributing influence in the development of this subdural hematoma. It seems logical to assume that there was no relation. The interval of seven years of absolute freedom of symptoms is against any association between the two conditions. The second point revolves about the fact that, both preoperatively and postoperatively, the patient denied any history of injury. Therefore, the question is again raised whether in cases of this sort blows of such relative insignificance that they are ignored or forgotten are sufficient to result in subdural bleeding. Patients suffering from deficiency diseases and alcoholism appear to be susceptible to the formation of subdural hematomas, and in many the evidence of trauma may be totally lacking. In the case presented above there was no evidence of deficiency or alcoholism; hence, insignificant trauma, which is often underestimated as an etiologic factor, seems to have been a reasonable causative agent.

Summary

From a series of 57 cases of cerebral hematoma, an unusual case of subdural hematoma with questionable etiology has been presented. The possible relation between brain abscess and such late complications has been mentioned, and the question of insignificant trauma as an etiologic factor has been raised.

27 Elm Street

A PHARMACOLOGIC AND CLINICAL RE-EVALUATION OF AMPHETAMINE (BENZEDRINE) SULFATE*

WILLIAM M. CAMERON, M.D.,† AND J. KASANIN, M.D.‡

SAN FRANCISCO

AMPHETAMINE (Benzedrine) has had a wide clinical application in recent years, but empirical enthusiasms have outraced and often ignored the experimental studies that might have tempered them. This extensive use of amphetamine has not generally been based on a commensurate pharmacologic knowledge of the drug and of the group of amines to which it is related. Consequently, many erroneous notions regarding the locus and mode of action of amphetamine are current. This is unfortunate because it tends to spread inaccurate conceptions of the role of the autonomic nervous system in the physiopathology of disease processes.

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Amphetamine is often called "sympathomimetic"; this is a misconception. The term "sympathomimetic" is a descriptive one meaning the mimicking of the effects of the sympathetic branch of the autonomic nervous system, "without," as Barger and Dale[1] have said, "involving any theoretical preconception as to the meaning of that relation [of action to sympathetic innervation] or the precise mechanism of action." Amphetamine mimics these effects to some degree, but there are important qualitative as well as quantitative differences between the actions of amphetamine and those of a truly sympathomimetic drug, such as epinephrine. Epinephrine reproduces all the effects of direct sympathetic stimulation because it activates the specific sympathetic effector mechanisms, and for this reason it is called "sympathicotropic." This elucidation of a more "precise

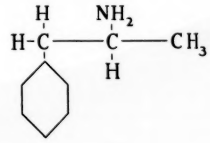
mechanism of action" is a development that has begun since the work of Barger and Dale, and is one that still remains incomplete. Amphetamine, however, is not sympathicotropic, and appears to act through direct stimulation of smooth muscle, and in other ways than through specific sympathetic channels. Similar misconceptions arose during the early experimental studies with tyramine[1, 2] and ephedrine.[3] A study of amphetamine should include a survey of the pharmacology of related sympathomimetic amines. These drugs may differ only slightly in their molecular configuration, and may nevertheless show considerable individuality in their actions; conversely, certain structural configurations determine important generic characteristics. Among these are certain toxic effects that must be watched for in the use of amphetamine, since all such effects have not yet been ruled out experimentally.

The stimulant effect of amphetamine on the central nervous system and its effective administration by mouth have probably promoted experimentation with the drug for other purposes. Yet its various peripheral actions appear to present no advantage over those of ephedrine and related compounds already in use. Indeed, when pressor, vasoconstrictor and other actions from amphetamine are sought, the central stimulant action confronts one as a serious disadvantage. Furthermore, it is a regrettable trend toward categorical thinking that forces some workers to class amphetamine as a sympathetic stimulant, and to equate it with epinephrine. Nor is its central stimulant action any evidence for general sympathetic stimulation, since the most typically sympathicotropic drugs do not possess this property.[4]

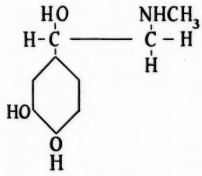
This paper presents a summary of the pharmacodynamics of amphetamine and related compounds, and considers chiefly the results of experiments on animals, since proper analyses can hardly be made with clinical material. The objectives of this survey are to establish some general correlations between molecular structure and action, as an aid in identifying the relation of amphetamine to the sympathomimetic amines; to aid in establishing more definite criteria of sympathicotropic action; and to stimulate a more critical attitude toward claims in this direction.

Pharmacodynamics*

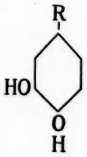
Amphetamine or phenylisopropylamine (dl-alpha-phenyl-beta-amino propane) is usually employed in the form of the racemic sulfate, except as an inhalant, when the carbonate is used. It induces general systemic effects when taken by mouth, inhalation or injection in doses of 2.5 to 10 mg. Its structural formula is as follows:



Epinephrine, the most potent of the sympathomimetic amines, is a typical sympathicotropic drug; its structural formula is as follows:



The structure of epinephrine meets the original criteria for optimal sympathomimetic activity postulated by Barger and Dale[1] and confirmed by many other workers.[5–10] It should be noted that epinephrine contains the catechol nucleus:



It is evident, however, that amphetamine departs from this optimal molecular configuration, and it will become clear that it does so at a sacrifice of its sympathomimetic effects, regardless of what other actions it may have acquired.

This assumed relation between structures and function may be checked by the classic experiments with ergotoxine and cocaine.[6] Tyramine,[11–13] ephedrine,[6, 14–17] phenylethanolamine[6, 18, 19] and amphetamine,[7, 20–23] all closely related structurally, fail to give to these tests the responses typical of sympathicotropic drugs. Functionally, then, they are only pseudosympathomimetic, and do not resemble epinephrine in their mode of action. Since the phenyl group of amines differs from epinephrine in both structure and function, it is of considerable significance that the addition of hydroxyl

*At the request of the Editors this section is presented in a summary form on account of its specialized nature.

groups to the phenyl ring of amphetamine,[22, 24] ephedrine[9, 10] and phenylethylamine[22, 24, 25] has in each case resulted in a sympathomimetic action more closely resembling that of epinephrine than was characteristic of the original drug. We may therefore conclude that the presence of the catechol nucleus, or possibly merely the meta OH-group, is necessary for sympathicotropic action. Variations in the side chain are of lesser significance. A longer side chain sacrifices intensity of action for greater duration, but carries greater toxicity. In the following summary of the effects of amphetamine on the various organ systems it would be well to bear in mind the comparison of these with the effects cited for other amines. If amphetamine seems neither more potent nor less toxic, it would be wise to advocate the use of one of the other amines.

Pressor Effects

Amphetamine has a pressor action in animals, although the effects are rather irregular and do not correspond closely to the dosage used.[20] Its ratio of activity to epinephrine is approximately that of 1:425,[7] and it is consequently classed as a weak pressor agent. It is exceeded in activity by ephedrine, tyramine and many other amines. Tachyphylaxis is probably more marked than with ephedrine, and in some cases even a second injection was ineffective or caused a fall of arterial pressure.[7] Its duration of effect is relatively prolonged.

The principal virtue of amphetamine in clinical use lies in its activity when given by mouth, in contrast to most of the other amines.[26, 27] Propadrine (phenylpropanolamine), however, might be worth trying when there are indications for the oral administration of a pressor drug. It is probably more active than either ephedrine or amphetamine,[7] is less toxic than ephedrine,[28] and because of its beta OH-group, is estimated to be one third as toxic as amphetamine.[27]

Cardiac Effects

Thienes and his co-workers[20] found that the heart in atropinized animals responded to amphetamine with a moderate increase in rate. There was no significant change in stroke volume. Chen and Schmidt,[3] Chen and Meek,[14, 15] and others[13, 29] have cited the depressant effect of ephedrine on the cardiac musculature. The possibility that amphetamine possesses similar undesirable effects must receive consideration. Chen and Meek[14] made electrocardiographic studies of dogs and rabbits that received large doses of ephedrine and found depression of the conduction system and various degrees of heart block. This was followed by ventricular fibrillation in some cases. It is significant that large doses of tyramine had no such effects. Phenylethanolamine is also relatively nontoxic to the heart.[18, 19, 22] Since a short side chain and the presence of an OH-group lessen toxicity,[22, 27, 28] a longer side chain, lacking an OH-group, has greater toxicity. Thus, the molecular structure of amphetamine conforms to the criteria for relatively high toxicity. Many workers[8, 22, 30, 31] have demonstrated that amphetamine and other phenyl amines are of little value in experimental circulatory collapse, and that the catechol derivatives are most effective. Clinically, Waud[32] has demonstrated cardiac depression in healthy young subjects following extremely large doses of amphetamine. Other workers have reported paradoxical falls in blood pressure during ordinary clinical use of the drug,[33–35] but few alarming cardiovascular effects have been cited.[36]

Bronchial Action

Clinicians have long been interested in finding an antiasthmatic substitute for ephedrine that could be effectively administered by mouth and would dilate the bronchi as well as ephedrine without the undesirable cerebral stimulation. Since amphetamine fails in the former condition, and exceeds ephedrine in the latter[37] it cannot be seriously considered as a bronchial dilator. Epinephrine and the other catechol derivatives far exceed amphetamine, ephedrine, tyramine and their structurally related amines in bronchodilator action.[8, 38–42]

Effects on Smooth Muscle

Both epinephrine and ephedrine inhibit intestinal motility. Chen, Wu and Henriksen[28] reported that the majority of twenty-four phenyl-ring derivatives, tested on isolated rabbit intestine, did likewise. Experiments with amphetamine have been less clear cut; Thienes and co-workers[20] have been unable to arrive at a formulation of the mode of action of amphetamine, although they have shown in nerve-degeneration experiments on the cat intestine that the modes of operation of amphetamine and ephedrine differ qualitatively from that of epinephrine.[21] Alles and Piness[23] obtained increased tonus with minimal concentrations of amphetamine, and relaxation with greater concentrations on the isolated rabbit ileum.

Myerson and Ritvo[43] believe that amphetamine is of decided value in relaxing gastrointestinal spasm of intrinsic or reflex origin, and that this relaxation occurs without a concomitant delay in gastric emptying time. Rosenberg, Arens, Marcus and Necheles,[44] however, obtained inconclusive clinical results with amphetamine, and in experimental studies found that the drug often induced

gastrointestinal spasm rather than relaxation. The conclusions of Beyer and Meek[45] also differed from those of Myerson and Ritvo: they found that amphetamine caused a delay in the final emptying time of the stomach, but that this effect was feeble as compared with that of atropine or ephedrine.

Mydriatic Action

Mydriasis may be produced by epinephrine, ephedrine, tyramine, amphetamine and many other amines.[3,13,19,46] There appears to be nothing unique in the clinical effects of amphetamine when used as a mydriatic, but denervation experiments clearly demonstrate that it is not sympathicotropic in action.[19,21] Caution should therefore be observed in drawing conclusions concerning physiopathology on a basis of its clinical effects.

Effects on Blood Sugar

Among the aromatic amines only epinephrine and related catechol derivatives possess the capacity to induce a rise in the blood-sugar level in nontoxic doses. Schaumann[9,10] has shown that the introduction of two OH-groups into the benzene ring — giving ephedrine a catechol nucleus — is enough to bestow the capacity to raise the blood sugar. Conversely, this highly specific sympathicotropic effect is lacking in drugs that have deviated as far as amphetamine from the molecular structure of epinephrine.[25,47,48]

Tachyphylaxis and Toxicity

Tachyphylaxis is that phenomenon in which a drug elicits progressively weaker responses in a succession of injections, although there is no apparent general physiologic decline to explain the fact. Pressor responses may even be reversed to depressor ones, and this may occur within three or four injections. Chen and Schmidt[3] described this phenomenon in their early work with ephedrine. It is common to most ephedrine derivatives, is present with phenylethylamine,[22] and is marked with amphetamine.[7] Tachyphylaxis does not occur with epinephrine and related catechol derivatives or with tyramine and phenylethanolamine.

It is evident that there is a close relation of structure to this important feature of drug activity. Amines that have long side chains and lack the OH-group, like amphetamine, show tachyphylaxis in its most marked degree. These structural features are also characteristic of the more toxic amines.

Chen and Schmidt[3] assumed that tachyphylaxis was caused by the cardiodepressant action of ephedrine, although the heart seemed quite responsive to subsequent injections of epinephrine. But Tainter,[49] using Gibbs's artificial heart in cats, demonstrated typical tachyphylaxis after ephedrine, proving that it was not entirely dependent on an altered response of the heart.

The most prevalent hypothesis seeking to explain the relation of tachyphylaxis to the structure of compounds like amphetamine and ephedrine is that these more stable compounds are not readily oxidized by the organism, and that consequently local fatigue occurs at their locus of operation, since they remain in the tissues until excreted by the kidneys. Since epinephrine operates on a different locus, it is still effective when the organism is fatigued by the action of these drugs. This failure to be quickly metabolized possibly explains their effectiveness when taken by mouth[26,27] and their generally more toxic nature, and is compatible with the more prolonged action of drugs like amphetamine.

Toxicity is best stated in terms of "therapeutic index" or ratio of toxic to therapeutic dose. The present study has shown that this index diminishes with the increasing length of the side chain and with the depletion of the amine of its OH-groups. The substitution of a propylamino-group for the methylamino-group in ephedrine, for example, results in the drug's manifesting only depressive and toxic effects.[28] It is evident from a consideration of its structure that amphetamine must be suspected of considerable toxic effect and a relatively low therapeutic index. The experimental studies cited have supported this conclusion. The use of repeated doses of amphetamine may lead to cumulative toxic effects, since the drug is not readily oxidized and is only slowly excreted through the kidneys.[50]

In many of the present applications of amphetamine, the central stimulation is a highly undesirable side action. In this respect the use of the drug for its feeble gastrointestinal effects is illogical, since its central stimulant action surpasses that of more effective drugs. It is not yet possible to say that in clinical doses amphetamine has no injurious effect on the heart. The collapse and death of a college student, recently reported by Smith,[51] suggest that accumulation may be a significant factor even when small doses are taken. The majority of cases of severe toxic reactions have occurred following no more than the therapeutic dose, and it is apparent that these patients were unusually sensitive to the drug. Nevertheless, since the widespread clinical use of amphetamine cannot be justified — except in certain conditions mentioned below — by the pharmacologic findings, it is unwise to risk even a remote chance of a grave toxic reaction.

Critique of Clinical Applications

A complete review of the present status of amphetamine therapy will not be presented, since this has been done recently by Davidoff and Reifenstein[33, 52] and others.[53–55] There is little doubt that the central effects of the drug have been very beneficial in narcolepsy,[37, 56, 57] in postencephalitic parkinsonism,[35, 58–60] and in alcoholic, barbiturate and some other intoxications.[52, 61] But its use in the psychotic states has not on the whole been encouraging.[34, 62–65] There has been little modification of the essential features of the schizophrenic or depressive reactions in cases treated with amphetamine. Occasionally patients appear more talkative and accessible, but these minor responses are just about balanced by panicky reactions and suicidal attempts in other patients. Wilbur, MacLean and Allen[53] obtained considerable but passing improvement in patients with so-called "chronic exhaustion" or mild depressive states. It is questionable whether one can consider this experience a specific response to amphetamine in any way analogous to the well-maintained responses in the patients with medical disorders.[37, 57] Nonspecific factors are difficult to control. Bahnsen, Jacobsen and Thesleff,[66] for example, found that of 100 normal adults comprising a control group in experiments with amphetamine, 13 per cent had lessened fatigue following the use of starch tablets.

Guttmann and Sargent[64] point out that amphetamine tends to exaggerate the innate personality trend, and may exaggerate hypochondriacal or obsessive reactions. They, and others,[53] have avoided its use in anxiety states, which tend to be heightened by the drug. Anxiety is a common component of many neuroses. One should consequently expect superficially satisfactory responses — decreased awareness of fatigue, talkativeness and mild hypomanic euphoria — to overlay a concomitant state of increased tension, potentially capable of involuntary and unintegrated expression. Panic states do occur, of course, and constitute an eventuality demanding constant vigilance in the use of amphetamine in the major reaction types. We are inclined to regard many of the disagreeable symptoms — palpitation, sweating and tremor — elicited by small doses in some normal subjects as manifestations of central rather than peripheral action, a central action that, in effect, mobilizes latent anxiety. Bahnsen et al.[66] also ascribed several of the peripheral effects of amphetamine to stimulation of the central nervous system.

Because negative findings are less apt to be reported than positive ones, we submit the following report. One of us (J. K.) has employed amphetamine* rather extensively in the psychiatric clinics of the Michael Reese Hospital in Chicago and of the Mount Zion Hospital in San Francisco, and can only conclude that the drug appeared to be of questionable value in the treatment of patients with psychogenic disorders. The conspicuous absence of either subjective or objective responses to doses of 10 to 20 mg. was quite common among these patients. Seventy-five patients, 36 men and 39 women, were so treated. Most of them were referred to the psychiatric clinics from other clinics of these hospitals, where they were complaining of nervousness, and where the functional nature of their symptoms became apparent to the examining physicians. Ten patients suffered from varying degrees of depression, whereas 65 showed symptoms of tension, insomnia, various somatic complaints with varying degree of anxiety, a feeling of insecurity, loss of faith in themselves, premonitions of dangers and death, and marked dependence on their physicians.

In the cases of depression, 3 patients showed a slight transitory improvement, but even then it was not possible to rule out other factors that might have been equally responsible for the improvement. The 3 patients who improved stated that amphetamine was responsible for giving them some "pep" to get up in the morning when they would otherwise prefer to stay in bed. It must be remembered, however, that together with the command to take the drug, the patients were told that they would feel very much better. Five patients reported no improvement, and 2 became definitely worse, complaining of feeling unnatural, giddy and "funny in the head," and getting more discouraged.

In the 65 patients suffering from neuroses, the suggestion that the drug would be very effective in ameliorating symptoms was used in 30, but only 9 stated that they felt better. Here one met with most paradoxical observations: 2 patients said that after taking amphetamine at night (by mistake) they slept very much better, and they asked that the drug be substituted for phenobarbital. Three patients said that they felt better and had more ambition than previously, but this lasted only a few weeks, after which they again became quite neurotic and complained of their previous symptoms. Four patients left the clinic, stating that they felt better, and did not respond to a follow-up letter. In the 35 cases in which the drug was given and no suggestion in any form was used, the patients reported no change. These patients were in the clinic for several months, were more or less stationary in their symptoms, and showed no response to various sedatives. It is quite possible that new patients who are given amphetamine at their first visit to the psychiatrist appear to re-

*Supplied through the courtesy of Smith, Kline and French Laboratories, Philadelphia.

act more favorably to the drug, but one must discount the effect of psychotherapy and not confuse it with the specific effect of the drug.

In general, in the light of our critical observations, there seemed to be no special indication for the use of amphetamine in either psychoneuroses or depressions. This was in marked contrast with the 2 cases of narcolepsy, in which a very dramatic improvement was similar to that reported by Prinzmetal[37] and Ulrich.[56] Dr. George S. Johnson,[67] director of the Psychiatric Department of Stanford University Hospitals, has informed us that in his clinic the experience with amphetamine was similar to our own.

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Summary

The molecular configuration of amphetamine (Benzedrine) places it in the group of phenyl amines, another member of which is ephedrine. None of the phenyl amines are truly sympathomimetic in their effects.

Amphetamine is not sympathicotropic in its mode and locus of operation, and consequently should not be equated with epinephrine.

Amphetamine is relatively feeble in potency in comparison with other aromatic amines, such as epinephrine, arterenol and tyramine.

It is clearly established that increased length of the side chain and the absence of OH-groups are associated with increased toxicity. By these criteria amphetamine must be suspected of relatively high toxicity, which can be ruled out only by further pharmacologic experimentation.

Because the toxicity of amphetamine has not been sufficiently determined and its action is relatively feeble, it seems preferable to employ other amines for peripheral effects on the cardiovascular, gastrointestinal and other systems.

Clinically, amphetamine is valuable in certain diseases of the central nervous system, such as narcolepsy and postencephalitic parkinsonism, and in certain intoxications. The administration of the drug in neuroses, depressions and schizophrenia seems of doubtful value, and may occasionally be harmful.

Favorable results reported in such heterogeneous states as orthostatic hypotension, chronic alcoholism, obesity and schizophrenia do not speak for specificity of action, but indicate rather that other variables (present in every therapeutic situation) may have contributed to the ultimate improvement of the patients.

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ENCEPHALOPATHY FOLLOWING NEOARSPHENAMINE THERAPY*

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CINCINNATI

THE occurrence of central-nervous-system reactions following the intravenous administration of the arsphenamines is infrequent, and the clinical and pathological pictures of these catastrophic states have not become clear to the physician. Smith and Newbill[1] in 1939 found 175 cases of arsenical encephalitis in the literature. Glaser, Imerman and Imerman[2] in 1935 made an exhaustive study of the literature to determine the frequency of so-called "hemorrhagic encephalitis and myelitis" secondary to intravenous arsphenamines. These authors collected 146 cases of encephalitis, 8 of myelitis and 4 of encephalomyelitis from a group of 191,125 patients who had received 1,108,778 injections of the arsphenamine compounds. The incidence of death due to central-nervous-system involvement was 1 in every 5398 cases, or 1 in every 28,768 injections. The mortality rate of patients suffering from arsphenamine encephalitis was 76 per cent. Glaser, Imerman and Imerman pointed out that these reactions occur also in nonsyphilitic cases and are apparently unrelated to the age and sex of the patient, to the quantity of the drug administered, to the number of injections given, or to the toxicity of the drug.

Toxic reactions in the central nervous system occur most commonly after the second dose (50 per cent in the series of Glaser, Imerman and Imerman), and usually develop from twelve to one hundred and forty-four hours after the injection. It has been noted[2] that only 0.5 per cent of the reactions occurred between the ninth and fifteenth injections.

We are reporting the clinical and pathological findings in a case of encephalopathy that occurred after the fifteenth intravenous injection of neoarsphenamine. This late reaction is quite unusual and merits consideration. The pathological picture presented differs somewhat from that characteristically described as "hemorrhagic encephalitis" following arsphenamine.

CASE REPORT

E. B., a 27-year-old married Negress, had been treated in various clinics of the outpatient department of the Cincinnati General Hospital since January 11, 1939, for many unrelated complaints, including vaginal bleeding, inability to become pregnant, tumor of the breast (a fibroadenoma was subsequently removed) and an infected dog-bite wound of the hand. Otherwise the general physical and neurologic status had been normal. On April 25, 1939, a blood Wassermann reaction was positive, although tests performed 1 year and also 1 month pre-

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viously in other hospitals had given negative reactions. Another serologic blood test, done on June 1, 1939, confirmed the positive result. On this basis, antisyphilitic therapy was begun. From June 19 to August 28, the patient received ten weekly intramuscular injections of bismuth (2 cc. of bismuth subsalicylate in oil). From September 1 to November 17 neoarsphenamine was administered intravenously at weekly intervals, each dose containing 0.6 gm. Another course of weekly injections of bismuth was then given from November 20 to January 22, 1940. From January 26 to February 23 neoarsphenamine was given weekly — 0.6 gm. to the dose. Thus by February 23, the patient had received the fifteenth injection of the arsenical.

On February 27, the patient was admitted to the hospital in a comatose state. An inadequate history was obtained from the employer. The patient had been in good health until noon on February 25, when she complained of slight headache and dizziness. She was unable to perform her duties as a housemaid. Later that day the headache became intense, and she went to bed. On the morning of February 27, she became delirious, and gradually lapsed into coma. She was then brought to the hospital.

The patient was unconscious, breathed stertorously, and was obviously seriously ill. General physical examination revealed a well-nourished and well-developed colored woman with a warm, dry skin and a generalized, mild lymphadenopathy. Examination of the heart, lungs, abdomen and extremities was essentially negative, and there was no cutaneous abnormality.

The obviously important findings were confined to the nervous system. The pupils measured 6 mm. in diameter and were equal in size and regular in outline. They dilated widely when a flashlight was shone into them, and then slowly contracted through a small range, despite the maintained light. The eyes tended to wander to the left but were quickly jerked back to the mid-line, with coarse, nystagmoid movements. The optic fundi were normal. There was, at times, increased resistance to passive movements of all the muscles of the trunk and extremities. These periods were marked by tonic extensor spasm, which lasted from 15 to 20 seconds. Following these episodes, muscular tone became notably decreased, and the respirations became slow and shallow. There was no spontaneous purposeful movement. The only response to painful stimuli occurred on severe supraorbital pressure, which caused the patient to grimace slightly. The tendon reflexes in the arms and legs were hyperactive bilaterally. The Hoffmann sign was strongly positive on both sides, and the plantar responses were flexor bilaterally. No abdominal reflexes were obtained. There was mild stiffness of the neck, but no Kernig or Brudzinski signs were elicited.

The course was steadily downhill. On the day following admission, the periodic tonic extensor spasm had disappeared. Muscular resistance and the tendon reflexes were normal and equal in all the extremities. However, Cheyne–Stokes respiration appeared, and death ensued in the early morning of February 29.

The temperature varied from 99.4 on admission to 100.8° F. terminally. The pulse rate ranged from 86 to 120, and the respirations from 22 to 36 per minute.

A lumbar puncture performed on admission revealed an initial pressure of 300 mm. of water. The cerebrospinal fluid was clear and colorless and contained 1 lymphocyte and 3 red blood cells per cubic millimeter. The Pandy reaction was +++, and the total protein 205 mg. per 100 cc. The cerebrospinal-fluid Wassermann reaction and gold-sol curve were negative. At a second lumbar puncture the following day a cerebrospinal-fluid pressure of 200 mm. was demonstrated. The fluid was clear and colorless, and contained no white cells and 8 red blood cells. The Pandy reaction was +; a quantitative protein determination was not done on this fluid.

The red-cell count was 3,910,000, and the white-cell count 5000. The differential picture was normal, and the hemoglobin 12.2 gm. The urine was normal.

Autopsy. The pathological findings exclusive of those in the nervous system were confluent lobular pneumonia with acute fibrinous pleuritis, acute bronchitis, left ventricular hypertrophy, severe toxic hepatosis and focal necrosis of the liver, acute splenitis, toxic nephrosis, early atherosclerosis of the aorta, mild pleural fibrosis, cystic right ovary, intracanalicular fibroadenoma of the breast, and leiomyoma of the uterus.

The right lung weighed 600, the left 275 gm. The right middle and lower lobes were swollen, and varied in consistence from a subcrepitant state to complete loss of crepitus. The lowermost portion of the middle lobe and the entire lower lobe on the right were dark red, mottled and irregularly friable on section. The remainder of the right lung and the entire left lung were normal, except for moderate congestion of the dependent portions of the latter. A section of the right lower lobe was removed with sterile precautions, and no pneumococcus could be identified from this material in the laboratory. Microscopic examination of tissue from the involved lobes confirmed the diagnosis of confluent lobular pneumonia. There were some signs of aspiration. All the evidence indicated that the pneumonia was of the hypostatic or terminal type.

Examination of the nervous system was limited to the brain, which weighed 1325 gm. The convolutions were moderately flattened and broadened, and the vessels of the meninges were congested. There was herniation of the uncus of the temporal lobe on both sides, more marked on the left. There was a well-defined cerebellar pressure cone, which, although small, was sharply indented, particularly on the left side. The vessels of the circle of Willis were soft, and the circle was of normal configuration.

The most notable feature of the sectioned brain was the presence throughout the white matter of discrete or confluent bright-red, pinpoint lesions, resembling petechiae. The tendency to symmetrical involvement of both hemispheres was striking (Fig. 1). Macroscopically it was noted that the gray matter of the convolutions and basal ganglia was not involved. The morbid process was widespread, extending from the frontal to the occipital poles, and it spared none of the lobes. However, the internal capsule and the corpus callosum were more extensively involved than other structures. The sectioned brain stem and cerebellum revealed only a few scattered petechiae in the cerebellar brachia.

Microscopically, the brain lesions consist of widespread and multiple foci of perivascular softening and demyelination. These are disseminated throughout the cerebral hemispheres, but are not found in the brain stem. These foci are present only in the white matter. In the center of the lesion there is a capillary or precapillary vessel with markedly swollen or completely destroyed endothelium. Immediately surrounding the central vessel there is an area of necrosis, which is relatively acellular, but in which a few macrophages with ingested pigment are noted. Pigment also lies free in these foci, and there are a few oligodendroglia and astrocytes in the perivascular spaces. Of course, these areas are denuded of myelin.

Surrounding these regions of necrosis is an occasional collar of neuroglia, composed of oligodendroglia and astrocytes. Only an occasional, recent, perivascular hemorrhage is seen in the subcortical white matter, internal capsule, corpus callosum and anterior commissure.

Vascular changes are widespread, and involve both gray and white matter, although they are more marked in the latter. The endothelium of some of the capillaries is hypertrophied so that, at times, the lumina are completely obliterated. Occasionally a thick hyaline thrombus completely occludes the lumen.

The changes in the nerve cells of the hemispheres and the brain stem are widespread and consist chiefly of moderate to severe chromatolysis. There is some glial proliferation. The leptomeninges contain no inflammatory reaction, but the vessels are moderately congested. There is no histological evidence of syphilis.

It has been suggested that this type of lesion in the nervous system may be associated with acute infection, and cases have been reported to support this thesis. Pneumonia was found at autopsy in this case, but the mildness of the infection clinically and pathologically seems to indicate that the encephalopathy was not based on this infection. There were no signs of pneumonia before death. The rectal temperature did not go above 100.8°F., and the white-cell count fifty-two hours after the onset and thirty-six hours before death was

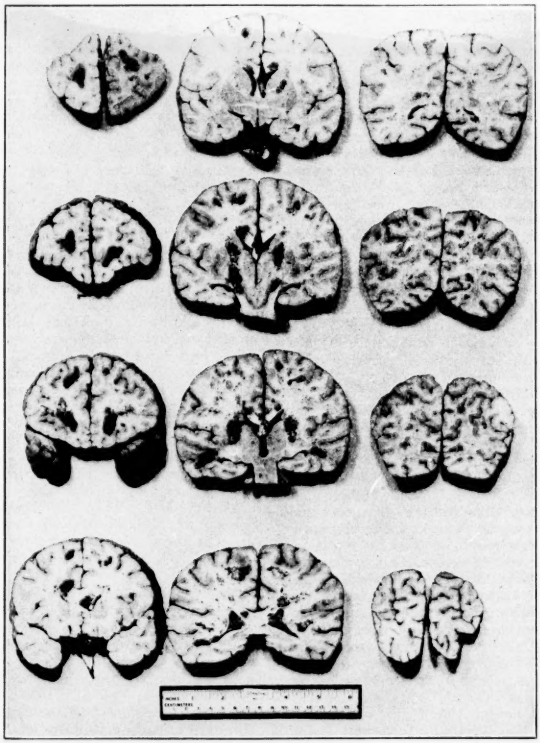

FIGURE 1.

Note the discrete, pinpoint and confluent lesions resembling petechiae, limited macroscopically to the white matter. The cerebrum was sectioned vertically into blocks 1.5 cm. thick. The position of the first block has been reversed to show the anterior extent of the process in the frontal poles. The corpus callosum was sectioned at autopsy to allow for better penetration of the formalin solution.

5000. Neither of these facts points to infection. The clinical signs were those of an overwhelming neurologic catastrophe that resulted in death eighty-eight hours after the initial symptom of slight headache. Nevertheless, the possibility that an acute infection was responsible for the encephalopathy in this case cannot be discarded.

The findings in this case deviated somewhat from the usual clinical and pathological descriptions of so-called "arsphenamine encephalitis." The unusual feature was the onset forty-eight hours after the fifteenth intravenous injection of neoarsphenamine. So far as we have been able to determine, there has been no authenticated case in which the disease occurred so late. As pointed out by Glaser, Imerman and Imerman,[2] Alpers,[3] and Russell,[4] the late occurrence of encephalopathy strongly suggests the possibility of sensitization of the cerebrovascular tree as the pathogenetic element, rather than the toxicity of arsenic per se, if this element is responsible.

The important pathological point was the occurrence of focal perivascular demyelinated areas of necrosis, widely distributed throughout the white matter of the cerebral hemispheres and largely unassociated with petechial hemorrhages. Russell[4] has pointed out that the necrotic foci do not represent a later stage of hemorrhage, but that the two processes, hemorrhage and perivascular necrosis, are quite independent of each other. Thus, the cognomens "brain purpura" and "hemorrhagic encephalitis" are in reality misnomers, for the hemorrhagic phenomena may play but a minor role. The blood-vessel changes were marked in this case, and were noted in the gray and white matter.

Summary

A fatal case of encephalopathy that occurred forty-eight hours after the fifteenth intravenous injection of neoarsphenamine is recorded. Confluent lobular pneumonia and toxic changes in the viscera were found at autopsy, in addition to the lesions in the nervous system. The most important lesions in the nervous system were focal perivascular areas of necrosis unrelated to hemorrhage. The perivascular necrosis was in relation to changes in the small blood vessels, chiefly of the endothelium, which not infrequently occluded the vessel. Petechial hemorrhages, which occurred probably simultaneously but apart from the perivascular necrosis, did not seem to be important in the analysis of the lesions of the disease.

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MEDICAL PROGRESS

TUBERCULOSIS

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DR. HENRY D. CHADWICK,[1] in his 1940 address as president of the National Tuberculosis Association, estimated that if the average decline of the last two decades can be maintained, the death rate from pulmonary tuberculosis in the United States will be 32 in 1950, 21 in 1960, 14 in 1970, 9 or 10 in 1980, and that "the bells that ring in the year 2000 may sound the death knell of the tubercle bacillus." In weight reduction, however, it is the last pounds that are the hardest to take off, and perhaps one should not expect to the last a steady decline in the death rate. In the meantime, there are wars and rumors of wars that may upset all calculations. It is therefore natural in this review to turn to the relation of tuberculosis to war, and since at present the United States is not fighting but assembling an army, the first problem concerns the detection of tuberculosis in the recruits for that army. Such a study outlines present methods of the diagnosis and control of tuberculosis.

TUBERCULOSIS AND THE UNITED STATES ARMY

As the United States begins its second draft of manpower in less than twenty-five years, one is appalled at the large number of patients with active or potentially active tuberculosis that were taken into the service in the draft of 1917, and the drain on the financial resources of the country that these cases have since become. The problem is very clearly stated by Spillman,[2] whose article is the source for the facts in the following four paragraphs.

The inadequacy of physical examination. It is difficult to realize how great a change has taken place in the diagnosis of pulmonary tuberculosis in the last twenty years. In 1917 the final criterion for determining the existence of active pulmonary tuberculosis was the presence of persistent post-tussal moist rales. This rule was adopted by the Army Medical Department on what it considered the best authority of the day. It is true that even at that time a few roentgenologists, particularly Dr. Lewis G. Cole, tried to induce the Surgeon General to make the roentgenogram and not physical signs the decisive factor in diagnosis; but the difficulty in obtaining enough imported glass plates, the cost of photography and the lack of trained roentgenologists seemed insuperable obstacles. Since then it has been proved that if one does rely on the discovery of rales, seven eighths of the early active lesions, as shown in the x-ray film, will be missed. Cole made a start in the collection of evidence of the superiority of x-ray diagnosis when in 1917 and 1918 he found that of 19 cases without physical signs but with x-ray evidence of pulmonary tuberculosis, at least 8 became heavy compensation liabilities because of the development of active processes.

The blame for many of the cases of tuberculosis taken into the Army cannot be placed, therefore, on the examining physicians but on the method of examination then in vogue. Nevertheless, one reads with surprise, that there were ". . . enormous numbers of health seekers whom the boards of the first draft sent, thinking that change of climate might benefit the manifestly tuberculous. . . ." This was obviously unfair to the Government and to the healthy comrades thus exposed to the disease, although it must be admitted that the danger of exposure in adult life was not appreciated then as it is now.

The cost of missed cases. In 1922, 36,600 soldiers received compensation for tuberculosis, and in 1939, 55,634, including 1947 deaths for that year. The approximate cost to the Government from 1917 to 1941 is as follows:

Cost of vocational training	$129,000,000
Insurance	130,000,000
Compensation	600,000,000
Hospital care	100,000,000
Total	$959,000,000

This does not include the cost of hospital construction. And Spillman points out an additional fact:

> Every month that goes by sees approximately three million dollars for compensation added to this bill. . . . It becomes a nice problem in accounting to estimate, from the foregoing data, just how much it costs to take a man into the service when he has tuberculosis. . . . I make it out somewhere around $10,000 per man to date, certainly not less than $7500, a figure to which can be added at least $50 a month for the rest of the

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man's life and compensation benefits for his dependents after his death.

The use of the x-ray in the present draft. Obviously no man with tuberculosis should be taken into the service, and the way to detect the disease is to x-ray the chests of all volunteers and draftees. Fortunately, such study is rapidly becoming part of the routine examination for admission to the Army. How many applicants will be rejected is not yet known, although the preliminary unofficial figures for Massachusetts reveal that to date only 0.6 per cent of the x-rays of 9000 recruits have shown tuberculous lesions, including active, suspicious and apparently healed ones, the three groups being about equal in size. Calcified childhood lesions are not included in these figures.

Statistics from the Canadian and Australian armies. Adamson[3] writes from Canada that as a result of ordering a chest plate of every recruit there have been 1.06 per cent rejections because of tuberculosis. He adds, "The general conclusion, namely, that 20 recruits will be discarded for every one of the population that dies each year of tuberculosis, is likely accurate." These rejections are necessary because experience during and since the last war shows that "for every 100 killed in action, 6 have died of tuberculosis; for each 100 pensioned for wounds, 25 have been pensioned for tuberculosis."

Cooper[4] reports that of 9000 recruits for the Australian army 1.33 per cent showed evidence in the lung fields of past or present tuberculous infection of the secondary adult type, whereas 0.55 per cent showed active pulmonary tuberculosis.

Case Finding in the Apparently Healthy Civil Population

The following studies on case finding in the civil population have been reported during the year. Plunkett and Mikol[5] report the results of routine x-ray examinations of 4853 adult admissions to fourteen general hospitals in ten cities of upstate New York during 1937 and 1938. In 128 of these, or 2.6 per cent, there was evidence of the reinfection type of tuberculosis. Of these, 51, or 1.1 per cent of the total, presented clinically significant lesions. In about half, tuberculosis had not been considered a possibility, and the survey revealed the first evidence of the disease. These and other published figures have been used as the basis for a campaign to make an x-ray examination of the chest of every patient admitted to general hospitals.

In a special supplement to the *American Review of Tuberculosis,* Edwards,[6] the director of the Bureau of Tuberculosis for New York City, writes on "Tuberculosis Case-Finding: Studies in mass surveys." Robins and Ehrlich[7] have summarized these studies in an article on "Group X-ray Surveys in Apparently Healthy Individuals." Their outstanding figures are the following:

High school students. Of 14,177 high school students with an average age of 16.5 years, 0.4 per cent had active lesions.

Home relief population of Harlem. In Harlem, 53,237 persons, predominantly Negro and Porto Rican, with an average age of 36.3 years, showed 3.1 per cent active and 1.0 per cent arrested tuberculosis.

Prison population. In 2477 prisoners with an average age of 38.7 years, four fifths of whom were men, 5.9 per cent active and 5.3 per cent arrested disease was demonstrated.

Homeless men. Among 3643 homeless, with an average age of 49.6 years, there was 5.2 per cent active and 10.9 per cent arrested disease.

Among the conclusions drawn were the following: In such studies the incidence of clinically significant pulmonary tuberculosis varies with the age, sex, race and economic level of the population studied. The greatest effort should be expended on adults and groups of low economic level. The majority of the cases, 70 per cent of the total, were discovered in the minimal stage. The incidence of active tuberculosis is lower in Negroes than in Whites among the apparently healthy population. This fact is surprising to most people, because the mortality rates for the Negroes by specified age and sex divisions are five to ten times those of the Whites, apparently owing to the fact that the Negro is more likely to develop acute exudative than fibrotic tuberculosis.[8]

Hedvall[9] reports a new study on the incidence of tuberculosis in university students. X-ray studies of 638 medical students at the Lund University in Sweden showed 11.3 per cent pulmonary tuberculosis. He believes, but does not prove, that a large proportion of these infections are contracted during post-mortem examinations. This possibility deserves further study.

Lyght[10] reports on college students in this country. In 1938 and 1939 he found that there were 165 colleges supporting case finding by tuberculin tests and x-ray study. In these colleges 348,713 students were checked, and 241 or 0.7 per cent demonstrated clinically active disease. In 117 colleges where there was no case-finding program, 129,851 students were enrolled, and only 4 active cases were reported during the year.

Reducing the Cost of Mass X-ray Examination

From the foregoing studies it is evident that one must look for early tuberculosis in the apparently healthy, but it is expensive to x-ray large

numbers. Therefore, much attention has been given to developing a cheap but effective method of x-ray examination. The following technics have been suggested and the results reported.

Fluoroscopy. The first method, and obviously the cheapest, is fluoroscopic examination. With the new fluoroscopic screen, a modern tube and an experienced observer, such an examination will bring to light almost all clinically significant cases, but a few potentially serious minimal cases will be missed. The best evaluation of this method is by Fellows and Ordway[11] of the Metropolitan Life Insurance Company, who state that in 1937, 2603 persons were examined by both fluoroscopy and standard x-ray films. The latter demonstrated pulmonary tuberculosis in 109 cases, in 14 of which the diagnosis had been missed on fluoroscopic examination, making the percentage of error 13. Of the 14 missed cases, "5 were latent or clinically insignificant, while 9 were considered clinically active." Another criticism of the fluoroscopic method is that it does not give a permanent record.

Miniature photographs of the fluoroscopic screen. Another suggested economy is to photograph on a small film the image on the fluoroscopic screen and thus eliminate the costly 14-by-17-inch standard film. Two sizes of film have been used for these fluorograms, the 35-mm. and the 4-by-5-inch. The camera holding the film has a special lens and is placed at the small end of a pyramid-shaped tunnel, with the fluoroscopic screen at the other end. The person to be x-rayed stands against the screen with the x-ray tube at the proper distance behind him. To ensure clear-cut shadows the fluorescent screen is seven times as fast as the usual Patterson screen. The cost of the complete equipment, including a $700 rotating anode tube, is $6000 to $8000. If there is already a complete x-ray installation, the extra equipment required — the tunnel with fluoroscopic screen and camera with special lens — costs about $2500.

Some investigators are enthusiastic about the 35-mm. film, but most agree that significant lesions are often missed in a small image that must be enlarged by a projector before it can be read. Present opinion favors the 4-by-5-inch film, which can be read without enlargement. Potter designed the apparatus and studied with Douglas and Birkelo[12, 13] 1610 clinic cases, using both the standard 14-by-17 and the 4-by-5-inch film for each case. With the standard method they found 271 active tuberculous lesions, 7 of which were not visible in the small films. The missed lesions were very small and were obscured by a rib in the small film. The percentage of error is, therefore, 2.6. In a test run, 73 persons were x-rayed in sixty-five minutes at a film cost of about one tenth that of the standard size. An additional argument in favor of the small films is the smaller space required for storage.

Aids in Interpreting the X-ray Film

Whatever the x-ray method, there will always be a significant number of asymptomatic cases in which the most experienced roentgenologist will have difficulty in determining whether the shadow is that of an active or inactive tuberculous process. Furthermore, even if the lesion is active from the histologic standpoint, will it heal without ever giving symptoms? So much has been published about the value of the differential white-cell count and the red-cell sedimentation rate in determining activity that a review of the salient points is in order.

Differential white-cell count. The value of the differential count of the white blood cells depends on the theory that the increase in the number of each type of cell in the blood parallels the predominance of that type of cell in the tuberculous lesion itself. Therefore, an increase in the large mononuclear cells in the blood is said to demonstrate new tubercle formation in the lungs, with large numbers of endothelial monocytes forming the tubercles. On the other hand, if the tuberculous lesion is healing, the number of lymphocytes in the blood will be increased because there is a collar of lymphocytes encircling the tubercles. Lastly, if there is cavity formation in the lung tissue, the influx of polymorphonuclears will be accompanied by an increase in these cells in the blood. Various authors give the numbers and relative numbers of the different white cells in percentages, in counts per cubic millimeter, in the monocyte-lymphocyte ratio, or by the Medler index, which is a single number calculated from the number of polymorphonuclears, lymphocytes and monocytes. In general, the rules given hold, but the great weakness in the method is that small active lesions may appear in the x-ray film and may increase in size for at least a few weeks before any change is evidenced in the differential count. It is true, also, that the cell count may be normal in the presence of advanced fibrocavernous disease with positive sputum.

Red-cell sedimentation rate. Active infection of any kind is usually accompanied by an increase in the fibrinogen content of the blood and a consequent increase in the sedimentation rate of the red cells. If, therefore, there is an active tuberculous lesion, the sedimentation rate should be increased in proportion to the severity of the infection. Again, in general, the rule holds; unfortunately, however, minimal active disease may exist without changing the sedimentation rate. It has been found,

too, that once the rate is elevated, it may continue thus long after the process is clinically inactive. For this reason one cannot always wait for a normal sedimentation rate before discharging a patient from a sanatorium.

Relation between the differential count and sedimentation rate. From the few cases reported, it appears that the first change shown in the blood after the beginning of tubercle formation is an increase in the large mononuclear cells, and that the change in the sedimentation rate comes later. Then as the process heals, the differential count returns to normal before the sedimentation rate.

Young polymorphonuclears. Without going into detail, the statement may be made (again with reservations) that an active tuberculous lesion is accompanied by an increase in the young polymorphonuclear cells in the blood. The difficulty lies in the determination of just what cells are young polymorphonuclears, and this makes the test unreliable except in the hands of an expert.

Blood studies and prognosis. A single blood study must be interpreted cautiously, but frequently repeated studies may have value in determining prognosis. Steady improvement in the blood counts may point to a favorable outcome before there is clear-cut regression of the x-ray shadow. On the other hand, in selecting patients for thoracoplasty some surgeons refuse to operate if there is an increasingly unfavorable blood change.

Examination of the fasting gastric contents. The value of examining the fasting gastric contents for tubercle bacilli has already been mentioned in previous reviews and recently in an editorial in the *Journal*.[14] Suffice it to say that the value of this examination is increasingly appreciated, and that the activity of a pulmonary process may often be proved by the finding of tubercle bacilli in the gastric contents of a patient without cough or expectoration.

Stiehm[15] has studied the blood and gastric contents of 40 subclinical cases, and concludes:

> Of available laboratory methods, the erythrocyte sediment rate was found to be normal in 90 per cent of the cases, and apparently gives little assurance that a lesion is either benign or inactive. The leukocyte reaction, where favorable, indicates a favorable prognosis. An unfavorable or equivocal leukocyte reaction, however, indicated an unfavorable course in only 50 per cent of the cases. Gastric aspiration with guinea pig inoculation is the most reliable method of proving both the diagnosis and activity of the lesion.

Development in X-ray Technic

So much is being said in the x-ray departments of large hospitals about "laminagraph," "planigraph" and "tomograph" that a word of explanation is in place.[16] These terms all mean that the new apparatus is designed to record the shadow of a specific plane or layer of the lung and eliminate the shadow of tissue in the other planes. The aim is to keep the focus on one plane while varying the focus on all other planes so as to blur their shadows. The film is exposed longer than in ordinary roentgenography, and both the tube and the film move in such a way that the purpose mentioned above is accomplished. The tube is located above the patient lying on the table, and moves in a plane parallel to that of the table. The film rests on a support under the table, and moves in the opposite direction from the tube. The two are joined in such a way that they move simultaneously. The plane desired in focus is at their fulcrum. Changing the level of the fulcrum makes it possible to x-ray successive levels of the chest.

The laminagraph is particularly helpful in demonstrating the large bronchi. Its main use in tuberculosis is to disclose cavities otherwise unseen because of overlying tissue. The real value of the procedure is yet to be established, and, of course, one of its drawbacks is the expense involved for the several films necessary to x-ray the different layers.

The Trend of Surgery in Tuberculosis

The policy followed in these reports is not to discuss new methods until their practical value has been established, but at times one is justified in pointing out certain trends. The belief that incision into a tuberculous pulmonary process must lead to a permanent bronchial fistula or chest-wall sinus has so long been accepted that recent surgical experiences to the contrary are worthy of note. In certain cases it has been shown that lobectomy, pneumonectomy and cavity drainage may be performed as successfully in tuberculosis as in other diseases. Such procedures may be indicated, especially when bronchial obstruction makes physiologic drainage through the bronchus impossible. The time has not yet come, however, to discuss indications, contraindications and technics.[17]

Minor Notes

Chemotherapy. Articles on the use of sulfanilamide and allied compounds in tuberculosis continue to appear. The studies, in the main, have been experimental and the results somewhat confusing. Thus far there is little hope that these chemicals will be of value in clinical tuberculosis.[18]

BCG. Vaccination with the Calmette-Guérin bacillus is still being tried abroad and to a limited extent in this country. The wisdom of such vaccination remains questionable.

Twelve-day guinea-pig test. Pickof[19] injects silica powder subcutaneously into a guinea pig, and then into the same area injects the material suspected of containing tubercle bacilli. In twelve days, if there is a firm infiltration, the material is removed by syringe and stained for tubercle bacilli. Since it is known that tubercle bacilli develop more rapidly in the presence of silica, the method holds promise.

The supposed waxy capsule. Lembke et al.[20] give evidence from ultramicroscopic observations on tubercle bacilli that the oft-mentioned waxy capsule of the bacillus is a myth, and that actually the wax is distributed throughout the structure of the organism.

X-ray changes preceding a positive tuberculin reaction. Evidence is accumulating that in certain cases the x-ray shadow of a tuberculous process precedes the positive tuberculin reaction.[21]

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Vol. 19

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27131

PRESENTATION OF CASE

First Admission. A thirty-nine-year-old man entered the hospital complaining of low-back pain.

Three years before admission the patient had had lobar pneumonia complicated by an empyema, which was drained by rib resection. A satisfactory convalescence followed, but ever since he had tired rather easily. During the year before admission he suffered from frequent infections, notably acute axillary abscesses for which incision and drainage were found necessary. He entered the hospital complaining of low back pain radiating down the right leg. It was of gradual onset and had been present for five days, but the patient stated that he had had many such attacks during the past nineteen years, the usual diagnosis being sacroiliac strain.

The patient had had an appendectomy twenty-two years before admission, and four years later an attack of jaundice with clay-colored stools; three years before entry, he had had a streptococcic sore throat.

On examination the patient was well developed and well nourished, somewhat pale and appeared chronically ill. Examination of the chest revealed a systolic scratch, which became accentuated during expiration and disappeared on inspiration in the third interspace immediately to the left of the sternum; the blood pressure was 140 systolic, 90 diastolic. Examination of the abdomen was negative. There was tenderness in the right sacroiliac joint, and all movements were limited here and in the right leg, because of pain. Examination of the nervous system was negative.

The temperature, pulse and respirations were normal.

Examination of the urine showed a ++ test for albumin. Examination of the blood showed a red-cell count of 2,690,000 with a hemoglobin of 53 per cent, and a white-cell count of 6300. The differential count was normal. The color index was 1.06, the volume index 1.08, the cell volume 25 per cent, the sedimentation rate 71 mm. in one hour. The nonprotein nitrogen of the blood serum was 24 mg., the protein 10.7 gm., the calcium 11.7 mg., the phosphorus 3.6 mg. per 100 cc., the phosphatase 6.8 Bodansky units, the total cholesterol 64 mg. per 100 cc.; the chlorides were 95.1 milliequiv. per liter. A blood Hinton test was negative. A bromsulfalein test showed less than 5 per cent retention of the dye in the serum; a formol-gel test was strongly positive; a phenolsulfonephthalein test was normal. A lumbar puncture gave an initial pressure of 250 and a final pressure of 200 mm. of spinal fluid after the removal of 10 cc. The cells were not increased, and the protein was 57 mg. per 100 cc.; the spinal-fluid Wassermann test was negative.

X-ray films of the spine showed some increased density about the articulation between the fifth lumbar vertebra and sacrum on the right side. The articulating surfaces were indistinct, and the density of the bone increased. There was no displacement and no narrowing of the intervertebral spaces. The other joints appeared normal. There were no changes in the structure of the bones.

Two weeks after admission a sternal puncture was performed, and it was found that 25 per cent of the nucleated cells in the marrow consisted of plasmocytes and plasmoblasts. Following this procedure, many unsuccessful attempts were made to demonstrate Bence-Jones protein in the urine. X-ray studies of the skull, cervical spine and long bones showed no variation from normal. During hospitalization an abscess developed in the left axilla and was incised and drained. The patient was given three blood transfusions, and discharged six weeks after admission, at which time the blood showed a red-cell count of 2,660,000 with a hemoglobin of 60 per cent and a white-cell count of 5000.

Second Admission (eleven days later). In the interval, x-ray therapy had been instituted and the patient felt a bit stronger, but still noticed palpitation and shortness of breath on exertion. Ten days after discharge he suffered a fainting spell, and hospitalization was therefore advised. The cervical, axillary and inguinal lymph nodes were palpable, and the spleen could just be felt on deep inspiration. The blood showed a red-cell count of 2,700,000 with a hemoglobin of 5.3 gm., and a white-cell count of 3700. Bence-Jones proteinuria could not be demonstrated. X-ray treatment was discontinued, and the patient was given one 500-cc. blood transfusion and discharged a week later.

Third Admission (three weeks later). Since leaving the hospital the patient had been confined to his bed most of the time, and shortly after returning home developed a severe nosebleed, which lasted for two days. Two weeks before admission he caught cold, and after a bout of sneezing a "red blurring" affected sight in his right eye, at first in the upper field, then gradually spreading over

the whole field of vision. In general he felt weak, and suffered from a right-sided headache and almost complete deafness in the right ear. On examination he had obviously lost ground and was pale and emaciated. Examination of the fundi showed many hemorrhages throughout all layers of both retinas with numerous patches of exudate. A well-circumscribed hemorrhage was present in the right macula. The cervical, axillary and inguinal lymph nodes were palpable, and those in the left axilla were still draining. A systolic murmur was audible over the entire precordium, maximal at the apex; the blood pressure was 114 systolic, 70 diastolic. The spleen and liver were just palpable. There was slight clubbing of the fingers. The blood showed a red-cell count of 1,340,000 with a hemoglobin of 25 gm., and a white-cell count of 4100. The differential count and the platelets were normal.

The patient remained in the hospital for approximately two months and during this time received fourteen 500-cc. blood transfusions. Six weeks after admission the clotting time and clot retraction were normal, the prothrombin time 16 seconds (normal 19 seconds) and a hematocrit reading 16.3. One epistaxis occurred, and blood films on two occasions showed 1 per cent atypical lymphocytes and 1 per cent blast cells. At the time of discharge the patient was symptomatically improved, but the blood showed a red-cell count of 1,410,000 with a hemoglobin of 45 per cent and a white-cell count of 1500.

Fourth Admission (six months later). On three occasions during the two months after discharge the patient was given a 500-cc. blood transfusion. He improved remarkably, lived a normal life and was free from symptoms until three weeks before admission, when he noticed dyspnea on exertion associated with a feeling of fullness in the upper abdomen.

On examination the patient appeared tired and was pale. The neck veins were dilated, and showed pulsations of both auricular and ventricular character. There was considerable enlargement of the heart, the sounds were of fair quality, but there was a slight gallop rhythm; the blood pressure was 120 systolic, 80 diastolic. The liver and spleen were not palpable, but the abdomen was tender in the liver region. There was no peripheral edema.

The urine showed a + test for albumin, but no Bence-Jones protein. The blood showed a red-cell count of 3,210,000 with a hemoglobin of 10.2 gm., and a white-cell count of 6700. The nonprotein nitrogen of the blood serum was 17 mg., the protein 7 gm. per 100 cc.

An x-ray film of the chest showed that the diaphragm was rather high on both sides but moved fairly well with respiration. The lung fields were of normal brilliancy throughout. The vascular shadows at both lung roots were increased in size and density. The heart shadow was enlarged in all diameters, and the apex was blunted; the greatest increase was to the left in the region of the ventricle. There were no visible mediastinal masses; the great vessels appeared normal.

Films of the abdomen showed the liver shadow fairly well; it did not appear to be greatly enlarged; the spleen was indistinct, but did appear to be somewhat larger than normal. The kidney outlines were visible and normal, or slightly increased in size. There was no evidence of a lesion in the bones. A Graham test was normal. An electrocardiographic recording showed a normal rhythm at 90. T_1 was upright, T_2 low and slightly diphasic with probably slight late inversion. T_3 showed late inversion, and Q_3 was rather prominent. The P waves and PR interval were normal. This was repeated at the end of deep inspiration and showed a normal rhythm at 85; T_1 was very low, T_2, T_3 and T_4 moderately inverted; R_4 was present.

The patient was discharged on the second hospital day.

Fifth Admission (two weeks later). The patient was given digitalis at home, but did not improve. Dyspnea was still present, and he suffered from an unpleasant sensation of pressure in the abdomen and chest. Anorexia and malaise developed, and he began to lose weight. Additional findings on physical examination were as follows: The cardiovascular abnormalities were as before, but the pulmonary second sound was now greater than the aortic. A few rales were heard at both lung bases, and the tender liver was 5 cm. below the costal margin. The blood picture was much the same, and the platelets were decreased.

An electrocardiogram showed normal rhythm at 95. The P waves and PR interval were normal. There was some slurring of the QRS complexes, and their duration was about 0.1 second. S_1 and Q_3 were prominent; T_1 was low, but upright, T_2 and T_3 inverted. There was a bizarre Lead 4, with ST_4 slightly elevated and T_4 diphasic and slightly inverted. During hospitalization the patient was given x-ray therapy totaling 1000 r in the three weeks.

Final Admission (two weeks later). In the interval the patient had gradually lost ground. At the time of entry he was weak and cyanotic and the neck veins very distended. The heart findings were unchanged except for an appreciable increase in the systolic apical murmur. There was dullness at the right base, and rales at the left

base. The liver was larger; there was no peripheral edema. The patient was given two more 500-cc. blood transfusions, but lapsed into coma and died on the ninth hospital day, approximately one year after his first admission.

Differential Diagnosis

Dr. Alfred O. Ludwig: There are many confusing leads in this case. I wonder if Dr. Holmes would show us the x-ray films, especially those of the spine and lungs.

Dr. George W. Holmes: I am quite familiar with this case, and I shall try not to give too much of it away. These films were taken because of pain in the back to see if there was a bone lesion. All that is described in the record is of no significance except for the statement that the spine showed increased density, and whether it actually does might even be questioned. The bones do seem more dense than one would expect in a sick person. Except for that, the x-ray evidence is of only negative value.

Dr. Ludwig: Is there any evidence of disease in the ribs?

Dr. Holmes: No.

Dr. Ludwig: I should like to ask if the marrow cavities seem increased in size.

Dr. Holmes: I think so, but that is a very unreliable finding, merely a guess. The skull is essentially normal.

Dr. Ludwig: Do these fine markings in the skull mean anything?

Dr. Holmes: I do not think so.

On the film taken at the fourth entry, there is definite evidence of variation in the heart and lungs. The heart shadow is increased in size. The apex is distinctly blunt, and the curve of the left ventricle is prominent. The enlargement is more to the left than in any other direction. There are also changes in the hilar region, and I think that the interpretation given was correct, that is, these changes were probably vascular and not neoplastic in origin.

Dr. Ludwig: Was there any definite evidence of tumor in the hilar nodes?

Dr. Holmes: There was no definite evidence of enlarged lymph nodes. I do not believe that one can absolutely rule out tumor. On the other hand, the appearance could be interpreted, along with the change in the heart shadow, as increased hilar shadows due to heart failure.

Dr. Ludwig: From the x-ray point of view, what should you say caused this condition?

Dr. Holmes: If I could dissociate what I know, I should say that it was the heart of hypertension.

Dr. Ludwig: Which, of course, the patient did not have.

Dr. Holmes: I think it is safe to say that the liver is enlarged. Here we see the spleen, certainly not very large, but on the borderline of being enlarged. The kidneys also look a little large. The patient was a rather small man, and the kidneys were not a long distance away from the film to account for magnification.

Dr. Ludwig: I think the kidneys should be large.

Dr. Holmes: So far as one can tell from the x-ray evidence, they are.

Dr. Ludwig: I have the impression that much of the evidence in this case is not very helpful in establishing the diagnosis that I think should be made. As I read this over I believed that the key to the correct diagnosis lay in the paragraph giving the laboratory findings. A number of things in that paragraph taken separately might not help, but taken together do. In the first place, albuminuria persisted throughout the illness; the patient had a normochromic, perhaps even somewhat hyperchromic, anemia; he had an extremely rapid sedimentation rate, a very definite hyperproteinemia of 10.7 gm., a slightly elevated serum calcium, a normal serum phosphorus and normal phosphatase, and a positive formol-gel test. The nonprotein nitrogen, chlorides, and liver-function and renal-function tests were within normal limits. I cannot explain the low cholesterol.

To go back to the story of back pain radiating down the leg, I first thought that it might be associated with the disease from which I believe the patient was suffering, and it may well be; but I do not believe if the attacks had been present for nineteen years that the two are related. A ruptured intervertebral disk might very well have caused these attacks. I have seen patients with ruptured disks in whom attacks persisted over such a period of time. The elevated total protein in the spinal fluid is confirmation, but there is no other evidence to allow that diagnosis.

In the second paragraph we are told that the sternal puncture showed that 25 per cent of the nucleated cells consisted of plasmocytes and plasmoblasts. This finding together with the clinical findings spell multiple myeloma in spite of the fact that there is nothing else to go with it. Albuminuria is extremely common in multiple myeloma — 75 per cent of the cases reported in the literature have it. The absence of Bence-Jones protein is disturbing, but it is present in only half the reported cases. The normochromic or hyperchromic anemia is found in 90 per cent. The slight hypercalcemia and normal phosphorus and phosphatase are also consistent. Most striking is the high serum protein, — 10.7 gm., — which is one of the most typical findings in multiple myeloma. It is

probably secondary to the elevation of the globulin fraction, which also accounts for the very rapid sedimentation rate and the positive formol-gel test. In addition, a high globulin content in the serum tends to cause clotting with Hayem's solution if that is used as a diluent in doing the red-cell count. Whether or not that was noted here I do not know. Dr. Holmes has already discouraged me from the x-ray point of view. I should have expected evidence of multiple myeloma in the bones, and we have none unless we can interpret increased marrow spaces in the long bones as secondary to tumor in this location.

This patient ran a course of anemia and increasing cardiac difficulty. We are told that a little later the spleen was palpable and that the lymph nodes became enlarged. In about half the cases of multiple myeloma recently autopsied here that Dr. Jacobson got together in 1929 the spleen was enlarged, and it is known that in multiple myeloma metastases to internal organs and also to lymph nodes may occur, although this is exceedingly rare. I do not know of any other condition that would give the sternal biopsy findings that we have in this case. If we grant that the patient had multiple myeloma, I think we still have a great deal to explain. What happened to him just before the third admission? The "red blurring," the deafness in the right ear, and right-sided headache, I should be inclined to account for on the basis of hemorrhage into the retina and also perhaps cerebral hemorrhage. We know that he had anemia and probably decreased platelets as well, which may have produced a tendency to bleed. The exudate in the retina is a little disturbing in that respect. The serum protein was normal on this admission. Perhaps Dr. Jacobson can tell us whether in any of his cases the protein returned to normal. I do not know whether that occurs in multiple myeloma.

Then we plunge into what is for me an unchartered field, — electrocardiography, — and I shall have to ask for help. I should interpret the findings as indicating a marked degree of myocardial damage. Can anyone help me?

Dr. Howard B. Sprague: It is difficult for me, as it is for Dr. Holmes, to dissociate myself from the knowledge of the case, because I came in through the back door of electrocardiography. I can only say that in the original interpretation of the electrocardiogram before I saw it, it was suggested that there was some myocardial coronary disease. We took special respiratory tracings to see whether we could change the direction of the T waves by change in the position of the heart, but the findings remained, and I suggested that they might mean pericardial disease — but I shall discuss that later.

Dr. Ludwig: Certainly, so far as I am concerned, this cardiovascular picture is very mysterious. Here is a man with a heart condition that looked as if it were due to hypertension, and he had no hypertension. It may be — if my original diagnosis of multiple myeloma is correct — that the renal changes associated with this disease play a part. However, I should expect, if that were so, that there would have been some hypertension. In some of the cases of myeloma with secondary nephritis, the patients have had hypertension, but in others it is absent. If this man had some other form of neoplastic disease, I should seriously suspect cardiac metastases. He died primarily a cardiac death, became increasingly weak, cyanotic and dyspneic, had dullness at the right base, rales at the left base, and evidence of enlargement of the liver and spleen, probably due to congestion. The kidneys probably were increased in size and may present the picture seen in these organs in multiple myeloma, a nephritis due supposedly to a plugging of the tubules with Bence–Jones protein. In summary, I think that one must make a diagnosis of multiple myeloma. I am unable to explain the cardiovascular signs and symptoms. It may be that the extensive radiation therapy accounted for the atypical course of the disease and the absence of bone changes.

Dr. Frank T. Hunter: Is it possible to find out whether that second serum protein of 7 gm. was done by the Kjeldahl or the specific-gravity method? We recently found in multiple myeloma that the specific-gravity procedure has no value. One can get a perfectly normal protein with that method and with the Kjeldahl method double it. I had one patient with a Kjeldahl value of 10 gm. and a specific-gravity value of 6.5.

Dr. William B. Breed: I will say that by the same process of thought and on the same basis of laboratory evidence we used myeloma as a working diagnosis through until the end. I think it is wrong to ignore the finding of these cells in the sternal smear. The smear was verified by Dr. Jacobson and Dr. Mallory. I think that something should be said about the x-ray treatment in this case. Dr. Holmes was interested in it, and although there had not been much success in the treatment of such cases with deep therapy, Dr. Holmes thought that it might be possible to change the situation from a rather acute one into a chronic one by x-ray therapy. The patient was given between December 21, 1939, and July 11, 1940, 1550 r by the quadrant technic, which includes the chest and the abdomen, once or twice weekly.

Then during the summer, following this treatment and fourteen transfusions, he had a remission. He had a happy summer and was well. The reason we stopped the x-ray treatment was that his blood was so low he had to have a transfusion once a week. We did not know exactly whether he got better because we stopped the x-ray or because he got delayed benefit from the x-ray therapy. Dr. Sprague saw him because of the electrocardiographic abnormality. He noted it in the laboratory and called me up to ascertain if this patient had pericarditis. I said that so far as I knew he had no pericarditis, but I asked Dr. Sprague to see him. We decided that he did not have it and went through the same process of thinking that Dr. Ludwig did in the question of whether he had some involvement of the heart or pericardium with tumor tissue. He was given x-ray treatment to the mediastinum — 1000 r between December 3 and 17 — on the basis that we might relieve some pressure that was interfering with the venous return; but to no avail. I refused to transfuse him further, and he died of a combination of anemia and cardiac failure.

Perhaps Dr. Holmes would like to say something more about the treatment.

Dr. Holmes: As Dr. Breed said, our diagnosis was multiple myeloma. That in itself is not a very favorable type of disease to treat by radiation. It is usually a generalized disease, and the area that one has to treat is so large that it is almost impossible to accomplish anything. Furthermore, it is not a particularly sensitive tumor, but if this patient had myeloma, it was certainly an atypical form. There was no involvement of the bone, which is one of the characteristic findings in the usual case of myeloma. We assumed that if it was myeloma, it was a very rapidly developing, very active type and for that reason might be more sensitive to radiation than the ordinary case. We had had some experience with leukemia, using this method of dividing the body into four areas and giving one quadrant, once a week, a rather small dose, taking eight weeks to go over the whole body. We consequently thought we were justified in trying it on that basis. As Dr. Breed said, we did not know whether we were successful in changing it into a more chronic form. The patient certainly had a good summer for some reason or other. We considered the danger of destroying what little blood-forming organs he had too great to continue, and we stopped.

Dr. Sprague: He entered with evidence of rapid enlargement of the heart, which could be checked against previous x-ray films. The electrocardiogram also could be checked against previous electrocardiograms that Dr. Breed had, and showed definite change. The patient had a big, dilated heart with gallop rhythm and evidence of both right-sided and left-sided failure of relatively mild degree at first. Later he presented more evidence of right-sided failure. However, in a general myocardial process the right ventricle generally fails first because it is the weaker chamber. The electrocardiogram was consistent with pericardial involvement, not necessarily pericardial fluid, and there was no definite evidence of constrictive pericarditis. There was the factor of anemia to account for the dilatation, and I thought the best bet probably was an infiltration of the pericardium, and perhaps the myocardium, by the underlying process, plus the anemia.

Dr. Bernard M. Jacobson: The serum protein of 10.7 gm., and several subsequent determinations were done in my laboratory by the gravimetric method, and were always high.

I have never seen a bone marrow with so many immature plasma-cell elements as this, suggesting something very acute or malignant. It is true that multiple myeloma is accompanied in many cases by spontaneous symptomatic remissions just as dramatic as the spontaneous remissions in pernicious anemia. It is impossible to explain them. Yet a patient may feel better despite the fact that the bone destruction seen by x-ray may be advancing all the time. One of the most difficult things for all of us to believe is that as many as 30 per cent of cases of myeloma, judging from a series of approximately 35 cases that we have studied, will have bones completely negative by x-ray study even at the time of death. One should certainly not hesitate to make a diagnosis of myeloma because the bones are normal.

Clinical Diagnosis

Plasma-cell myeloma.

Dr. Ludwig's Diagnoses

Multiple myeloma.
Cardiac failure.
Ruptured intervertebral disk?

Anatomical Diagnoses

Plasma-cell myeloma, diffuse.
Probable reticulum-cell sarcoma of the femoral marrow.
Pulmonary endarteritis.
Cor pulmonale.
Adhesive pericarditis.
Pulmonary edema.
Chronic passive congestion of liver, spleen and kidneys.

Pathological Discussion

Dr. Tracy B. Mallory: I am sorry time is short, because I am sure we should all like to continue this discussion. The autopsy showed a considerably enlarged heart, weighing over 500 gm., and an adhesive pericarditis. The adhesions seemed relatively recent. They could be stripped away by blunt dissection for the most part, and there was none of the marked thickening that one sees in the pericarditis of Pick's disease. I personally found it hard to believe that the pericardium could have been responsible for the cardiac failure. We see this degree of adhesive pericarditis too frequently in patients without cardiac symptoms. The thing that impressed me at the time of autopsy was the dilatation of the right ventricle and especially the dilatation of the pulmonary conus. Despite its dilatation, the right ventricle measured 5 mm. in thickness. I therefore felt justified in making a gross diagnosis of cor pulmonale. The lungs were very large and extremely wet and edematous. Grossly we could not find any atheroma in the pulmonary arteries; microscopically, however, all the minute pulmonary arteries showed an obliterative endarteritis. I have little doubt that the immediate cardiac difficulty was a cor pulmonale, secondary to pulmonary endarteritis. When the endarteritis developed, I have no idea. It is conceivable that radiation might have been the cause, but the amount of x-ray treatment was hardly great enough to make that probable.

The liver was very much enlarged, weighing 2500 gm., and showed the most extreme grade of congestion, with hemorrhagic necrosis of at least three quarters of every lobule, only a few viable liver cells persisting at the periphery. The spleen was enlarged also by passive congestion. The kidneys together weighed 600 gm., mostly due to edema. There were no casts in the tubules and nothing to justify a diagnosis of so-called "myeloma kidneys." I should like to inject a word of caution regarding interpretation of puzzling findings in cases of myeloma by the assumption of extraosseous myelomatous infiltrations. They are of extreme rarity. We have never seen any of significant degree in this laboratory. Compensatory hematopoiesis would be a more likely cause of enlargement of liver or spleen.

The proof of a diagnosis of myeloma must come, of course, from examination of the bone marrow. The picture in this case was rather puzzling and raises many questions, which I cannot answer.

An abnormal number of plasma cells were present in most of the sections studied, but in none was the proportion greater than 10 to 15 per cent of the nucleated cells, whereas in the original bone-marrow aspirations they made up 25 per cent. In the intervening period they had apparently decreased rather than increased. This may have been the result of the radiotherapy, and might be interpreted as evidence of success. On the other hand the patient's anemia after a temporary remission had grown more severe. I have always assumed that the mechanism of anemia in cases of myeloma was that of progressive replacement of the hematopoietic marrow by tumor cells, a myelophthisic anemia. Certainly that was not the case here. The normal marrow elements were not decreased in number although they did show some shift to the left in differentiation. Even the marrow fat was not greatly decreased in amount. I believe we must conclude that this patient had myeloma, but I do not believe that we can attribute his death directly to it.

A further puzzle was added by a section of the femoral marrow. This had been noted to be deep red on gross examination. Microscopically it appears neoplastic, but the cells are certainly not plasma cells or their derivatives. They appear for the most part to belong to the clasmatocytic group, though a very large proportion of them are multinucleated. I am in doubt how this should be classified but believe it falls closest to the reticulum-sarcoma group. We found no evidence of similar neoplasm in any of the other bones examined, but six bones do not constitute a very large proportion of the human skeleton, so that we really do not know how extensive it may have been.

CASE 27132

Presentation of Case

A sixty-one-year-old business man complained of substernal pain.

The patient was perfectly well until three days before consulting his physician, when he was seized with a severe substernal pain, which radiated down both arms to the wrists, where it produced considerable pain. The attack lasted from thirty to sixty seconds, then subsided and the patient felt quite well again. Exactly similar pains occurred from five to ten times a day during the next three days before he sought advice. It was unrelated to effort and occurred with greatest intensity at about three o'clock in the morning, when it awakened the patient. He felt perfectly well between times, and there was no dyspnea, orthopnea or cough. The patient was a tense, highly strung and active business man.

The past and family histories were irrelevant.

Physical examination was entirely negative, including the heart, which was not enlarged to per-

cussion. The sounds were regular and of fair quality, the rate 74, and there were no murmurs. The blood pressure was 130 systolic, 80 diastolic.

The patient remained in bed for the next three days, but the attacks did not decrease in number and remained unrelated to effort; the effectiveness of nitroglycerin could not be determined because of the short duration of the pain, but it did appear to abort a few of the longer attacks. He reported to his physician at the end of this time, and physical examination was again entirely negative. Examination of the urine and blood was negative, and a blood Hinton reaction was negative. An electrocardiographic recording was normal.

The patient continued to have these attacks. At midnight two weeks later he awoke with a severe agonizing substernal pain radiating to both wrists. His physician was summoned some five hours later, and it appeared that the patient had been sitting in a chair writhing in agony during this time. His skin was white, and he was obviously in extreme pain. Even then the only change in physical examination was a much poorer quality of heart sound; the blood pressure was 120 systolic, 80 diastolic, the pulse 70. One-half grain of morphine gave great relief, and the patient dropped off to sleep. Three hours later he became cyanotic and developed a cough, rales being heard throughout both lungs. Digitalization was started, but the patient suddenly died fourteen hours after the onset of pain.

Differential Diagnosis

Dr. Sylvester McGinn: This case is rather unique for these exercises in that there is not a single abnormal physical or laboratory finding to help in making the diagnosis. At least it emphasizes the importance of history in any cardiac examination. I presume the diagnosis could have been made about as well over a telephone as it could at the bedside. The syndrome of angina pectoris with some typical and atypical features runs through the entire history. We have a man who had apparently always been in good health and suddenly was overcome with an illness, which from the very beginning had the earmarks of being very serious and within three weeks caused sudden death, a death that from the nature of the symptoms might well have been anticipated.

Among the causes of sudden death in a man of his age, although there is nothing particularly in the record to indicate it, would be dissecting aneurysm. The pain in this case was not one to suggest it. The patient had neither back pain, abdominal pain nor pain in the legs. Furthermore, it is unusual to find dissecting aneurysm in a patient without hypertension. Pulmonary embolism could cause sudden death, but here we have a man suffering five to ten attacks a day for a period of weeks, and that does not sound like pulmonary embolism, nor did he have a pleuritic type of pain. Angina decubitus with a gradual and impending coronary occlusion seems to me to be the most likely diagnosis. The term "angina decubitus" means a very severe angina with attacks occurring even when the patient is at rest. Such cases are quite uncommon. We see them in syphilitic heart disease, but this man had a negative Hinton reaction. I have seen several cases with severe anemia associated with coronary sclerosis, but this man's blood study was negative. Some patients with aortic stenosis may have angina decubitus, but physical examination of the heart in this case was normal, so that I think we must rule out a valvular disturbance. In trying to reconstruct the case, it seems to me there was a small, partial coronary occlusion and finally the occlusion became complete either by dislodgment of an atheromatous plaque or a gradually increasing thrombosis. I assume that complete occlusion occurred at the final episode, when he died. Had it occurred prior to that time we should probably have found definite evidence of myocardial infarction, either in the physical findings or in the electrocardiogram that was reported. These negative findings would rule out myocardial rupture as the final cause of his demise. I should like to make a diagnosis of coronary sclerosis with coronary occlusion, and angina pectoris with an impending complete occlusion.

Dr. Howard B. Sprague: Should you like to suggest that he had a process in the right coronary artery, because he had pain in the right arm?

Dr. McGinn: Not with a normal electrocardiogram.

Dr. Alfred Kranes: There are several points of interest in the story. The first is the suddenness and severity with which it started. The patient insisted that he had been quite well previously. Several months before he was seen, he had applied for a large insurance policy and had passed the physical examination successfully. That fact might, I suppose, make one slightly suspicious that the history might not be entirely accurate. At any rate, the insurance company feels that way about it. The second point is that the pain was not related to effort. He could run up a flight of stairs without any difficulty but had a good deal of pain lying quietly in bed at night. Finally the electrocardiogram taken ten days before his death was entirely normal. I am sorry I did not bring it with me.

Dr. Sprague: A person, of course, can have a

complete occlusion of a coronary artery with a normal electrocardiogram and then suddenly occlude the other one and die, because the entire coronary circulation has been cut off. In regard to the insurance aspect, recently an insurance man told me that it was well known that as soon as a diagnosis of angina pectoris with normal electrocardiograms has been made the patients frequently take out life-insurance policies.

Clinical Diagnoses

Angina pectoris.
Coronary thrombosis.

Dr. McGinn's Diagnoses

Coronary sclerosis.
Coronary occlusion.
Angina pectoris with impending occlusion.

Anatomical Diagnoses

Coronary thrombosis, left descending branch.
Infarct of left ventricle with rupture.
Hemopericardium.
Mural thrombus, left ventricle.
Acute passive congestion.

Pathological Discussion

Dr. Tracy B. Mallory: At autopsy the pericardium was discolored and enormously distended, and on incision nearly 1200 cc. of blood escaped from it. On examining the heart it was obvious that there was a soft spot occupying about one third of the apex, in the center of which the necrotic muscle fibers had separated sufficiently to admit a fairly large probe. On the ventricular surface of the infarct there was a large thrombus. The exact age of the infarct was difficult to determine. It was certainly more than a week old, and I think it may possibly have dated back to the onset of symptoms, a little over three weeks' duration. Rupture of the heart, however, usually occurs within the first two weeks after infarction. The left descending coronary artery showed a fairly fresh, completely occluding thrombus with underlying atheromatous changes. The other arteries were all quite patent, so that this apparently was a case of infarction based on occlusion of a single coronary vessel. Except for a very acute pulmonary and generalized passive congestion there was nothing else found.

Dr. Kranes: Do you think that was present when the symptoms began?

Dr. Mallory: Yes. I do not believe we can be dogmatic about the duration, but I believe we can say more than a week and very likely between two and three weeks.

Dr. Kranes: That being the case, it must have been present ten days previously, when the normal electrocardiogram was taken.

Dr. Mallory: I think it almost certainly was.

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NATIONAL CANCER MONTH

This year, with attention distracted by world turmoil, it is all the more necessary to have some specific event to focus interest, at least in passing, on cancer and its relation to human beings, since this problem — war or no war, emergency or no emergency — is always with us. Hence, it is appropriate that April has been set aside as National Cancer Month.

During the coming year it is to be hoped that the progress made in this field in previous years will continue. However, it is all too easy to forget that the problem is far from solved and that, in the need for airplanes, tanks and submarines, the less spectacular necessity for continued effort against cancer persists. The very fact that Massachusetts has in recent years been showing a falling death rate from this disease is all the more reason to intensify efforts to overcome it.

Year by year, advance in knowledge of the treatment not only of cancer itself but also of precancerous conditions has increased, and there is now more than a glimmering of hope that a fair proportion of cutaneous cancers, and even some cancers of the uterine cervix, may be prevented by adequate care of certain types of premalignant lesions.

Additional experience in the field of high-voltage and super-voltage radiation therapy, the use of the new radio-active isotopes and the advances made in the field of thoracic surgery have provided further means by which various forms of cancer may be more successfully treated.

Education to permit the application of this therapy early in the development of a neoplastic process is an essential part of any effort to meet the problem. The willingness of the medical profession to aid in this educational work has been and must continue to be an important factor in reducing mortality from cancer.

THE TREATMENT OF THE PSYCHONEUROTIC

The principal forms of treatment now in vogue for the psychoneurotic patient, evolved through centuries of experience, are the "psychobiological" approach, advocated and developed in America by Adolf Meyer, the "persuasive" method of Dubois and the "re-educational" form, exemplified by the work of the late Austen Fox Riggs and often spoken of as the "Stockbridge method." All these procedures have their adherents in the treatment of the largest group of patients seen in medical practice. Success is claimed for each one or for various combinations. Few analytic evaluations of the results have, however, been reported, and the importance or unimportance of any one method is vaguely delimited in the minds of most physicians. How would a group of patients treated by the Meyer method compare with a similar number under the guidance of the re-educational form of Riggs, or the persuasive method of Dubois? No one knows, since no such analyses have been made.

For one type of treatment, however, that of Riggs, data are now available.* Such reviews are needed of all "systems," for it is largely by analysis of the results that a rational conclusion can be drawn regarding the effectiveness of treatment.

The Stockbridge method is based on certain concepts of the psychoneuroses as understood by Riggs. A constitutional vulnerability was considered the basic etiologic factor, made up of two main components, "a marked imbalance of the instinctive drives and a high degree of hypersensitivity, deep-rooted characteristics which profoundly influence the quality and intensity of the individual's habitual responses and predispose him to psychoneurotic illness." The hypersensitive person, especially if subjected to early unfavorable environmental influences, tends to develop distorted values, impractical ideals and faulty attitudes and habits. Immaturity of thought and action is the commonest factor; inner struggles, discordant relations, anxiety, insecurity, distressing feelings and many other symptoms may result.

With such a basis for a psychoneurosis, the Stockbridge treatment consists, in brief, of an attempt to aid the patient in obtaining insight into the development of his disorder by means of a painstaking personality review — usually by straightforward discussion. After a fair measure of insight is obtained, rehabilitation is attempted by weighing the useful against the unsatisfactory patterns of response. Finally the patient is tested against a normal background by living with his fellow men in an unrestricted environment.

To evaluate the results of treatment, a statistical study has been made of more than a thousand patients treated at Stockbridge during a twenty-five-year period from 1910 through 1934. The data coded were based on case histories, and it should be noted that only 4 per cent of the histories were thought to be excellent, 10 per cent good, 50 per cent fair and 37 per cent meager. To this was added information received after discharge of the patient in 96 per cent of the cases. In the estimates of the level of adjustment reached by all the patients, 34 per cent were described as good, 48 per cent fair, 14 per cent poor and 4 per cent unknown. Thus a third made a good recovery, and over four fifths a good or fair recovery. Considering the fact that the median length of the first visit to Stockbridge for women was only thirty-four days and for men only twenty-six days, although the total duration of treatment in the majority of cases, owing to return follow-up visits, was much longer, the results of therapy may be said to be good. The chief weakness of the survey, however, lies in the relatively poor case records, a fault that should be overcome in the future.

One cannot estimate the value of the Stockbridge method as compared with other methods of treatment, since no satisfactory standards have been set up by other clinics. A beginning has been made in the Stockbridge survey. It is expected that others will follow the excellent example set by Coon and Raymond.

*Coon, G. P., and Raymond, A. F.: *A Review of the Psychoneuroses at Stockbridge*. 299 pp. Stockbridge, Mass.: Austen Riggs Foundation, Inc., 1940.

MEDICAL EPONYM

Haygarth's Nodosities

Haygarth's nodosities were described by John Haygarth (1740–1827), F.R.S. and F.R.S. (Edinburgh), in his book, *A Clinical History of Diseases* (Vol. II, p. 155; London, 1805). The section containing the following excerpt is called "A Clinical History of the Nodosity of the Joints."

> In this disease the ends of the bones, the periosteum, capsules or ligaments, which form the joint, gradually increase. These nodes are not separate tumours, but feel as if they were an enlargement of the bones themselves. . . .
>
> The Nodes appear most nearly to resemble Gout. Both of them are attended with pain and swelling of the joints: but they differ essentially in many distinguishable circumstances. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MEDICAL EDUCATION AND MEDICAL DIPLOMAS

The Council at its meeting May 21, 1940, directed the Committee on Medical Education and Medical Diplomas to submit to it changes in the by-laws relative to the method of admission of the graduates of unapproved medical schools to the Society. While engaged in this task the com-

mittee thought that certain other matters not directly in line with the above purpose, but more or less related to it, should be included in the changes to be submitted. Following are the report and recommendations as submitted to the Council at its meeting on February 5, 1941. It was decided at that meeting that the report should be printed in full with appropriate comments, so that the whole matter might be more carefully considered at a special meeting of the Council to be called for that purpose. Explanatory comments for which the chairman of the committee is solely responsible have been inserted after each suggested change in the by-laws.

* * *

For several years among the applicants for fellowship in the Society the number of graduates of medical institutions not on the list recognized by the Council has been increasing. At the present there are two groups of such graduates. One, and much the larger group, is composed chiefly of graduates of domestic institutions not recognized as medical schools by the American Medical Association. This group also includes a few American-born graduates of foreign medical schools, who have studied abroad, usually because they were not accepted by any recognized domestic medical school. There are a few foreign-born, foreign-educated physicians in this group who have migrated to this country, chiefly before 1937. The other group, much smaller than the first, is composed almost entirely of foreign-born graduates of foreign medical schools who are chiefly German and Jewish, but by no means exclusively either. Most of these physicians have migrated recently to this country primarily to escape political oppression. Almost without exception, they have had a good medical education and are of proved ability, often being older men of outstanding ability with international reputations.

The members of the Committee on Medical Education and Medical Diplomas are unanimous in believing that it is in the best interests of this Society to treat these two groups differently. The basis of this difference we believe should be whether or not an applicant has had an adequate medical education and enjoys a good professional reputation. With very few exceptions the members of the first group have had an inadequate education, those of the second an adequate one, and it is usually not difficult to distinguish between them. We believe that members of the first group should be admitted to membership only when there is ample positive proof that they can be regarded as truly desirable additions to the Society. At present, in the absence of evidences of undesirability other than an inadequate medical education, they are assumed to be desirable. We cannot agree with this attitude. We believe the members of the second group should become members of the Society as soon as they have been long enough in this country to have created definite favorable opinion in the minds of colleagues whose judgment would be commonly considered valuable.

The committee has been unable under the present system to evaluate adequately the desirability for fellowship of the majority of candidates appearing before it. Repeated attempts to gather information about the prospective candidates from the officers and fellows of the district societies have usually failed. A typical situation is for an applicant who is a graduate of an unrecognized domestic school to appear before the members of the committee, who have never seen him before, but who must decide as to his desirability from his appearance, diploma, application blank and a sheaf of letters personally solicited from his medical acquaintances, who invariably say that the applicant "is a capable and conscientious practitioner of medicine" and that his practice is "ethical." Only rarely has the committee received what it regards as a confidential expression of honest intelligent opinion regarding an applicant and his work from colleagues who really know him. Part of the present functioning of the committee as dictated by the by-laws has become farcical in the minds of its members. A major change in this undesirable situation seems impossible under the present by-laws.

The Committee therefore recommends that the following changes be made in the by-laws:

1. The name of the committee be changed to the Committee on Medical Education. *(The Committee on Medical Diplomas was created in 1881 primarily to make a periodic revision of the list of medical schools recognized by the Council. The Committee on Medical Education was created in 1906 primarily to consider improvement of state laws regarding registration in medicine. The two committees were combined in 1913. The present chief function of the Committee on Medical Education and Medical Diplomas is to investigate the qualifications of applicants who are graduates of unrecognized schools. The change is recommended only in the interest of simplification.)*

2. *Chapter 1, Section 1:* In line 5 on page 9 delete the clause, "that their names and addresses . . . prior to their examination by the censors;". *(This clause appears more appropriately elsewhere. See Recommendation 9.)*

3. In line 10 on page 9 omit the words, "or college". *(It seems unnecessary now to use the terminology "medical school or college", though it once might have had some legal reason. The change is recommended only in the interest of simplification.)*

4. In line 14 on page 9 after "code of ethics of this Society;" insert "that they have made application according to the provisions of Chapter V, Section 2; that they have paid the examination fee of three dollars;". *(The ultimate responsibility of seeing that all new applicants comply with the various provisions for entrance into the Society should rest with the censors. Article 3 of the constitution of the Society reads in part as follows, "No person shall become a member of the Massachusetts Medical Society except upon examination by the censors of said society . . . ." The contents of these two clauses are discussed under Recommendations 9 and 8 a respectively.)*

5. *Chapter I, Section 6:* In line 5 on page 10 substitute the word, "December," for "November." *(The date of the present fall censors' examination is the first Thursday in November. According to the new "time-table" set up under Recommendation 9 the first Thursday in December seems better, as otherwise the closing date for applications from graduates of unapproved schools falls too close to Labor Day, an admittedly poor date for district secretaries and applicants alike. No such change in the date of the spring examination is needed.)*

6. *Chapter V, Section 1:* Beginning at line 11 from bottom of page 16, delete the whole paragraph, "Diplomas from medical schools . . . to take an examination." *(The contents of this paragraph appear more appropriately elsewhere. See Recommendation 9. The only factual change is in the period of time.)*

7. In line 2 from bottom of page 16 substitute the word, "December," for "November." *(See Recommendation 5.)*

8. At the bottom of page 16 insert the following: *(a)* "A fee of three dollars shall be paid by an applicant for fellowship to the district secretary for deposit in the funds of the general Society before each examination or re-examination by the censors. *(b)* An applicant shall not be considered as possessing the requisite qualifications for fellowship unless approved by at least three censors. *(c)* An applicant failing two examinations shall be disqualified from again applying for fellowship until three years have elapsed from the date of the last application."

(a. Examination by the censors of applicants for fellowship at present involves the applicant in no expense. The censors, however, are paid for their work, as provided for in Chapter V, Section 4, of the by-laws. In accordance with the usual custom of institutions of learning, learned societies and boards of registration in medicine everywhere it is felt that the Society should charge a fee for its examinations.

b. Unchanged.

c. If an applicant is not passed by the censors at two examinations, it is believed that some time should elapse before re-examination, so that an applicant may improve his qualifications and not appear at every examination with essentially unchanged qualifications.)

9. *Chapter V, Section 2:* To read as follows:

(a) "An applicant for fellowship who is a graduate of a medical school recognized by the Council shall apply on a form furnished for the purpose to the secretary of the district in which he has legal residence, not later than March 1 for the May censors' examination or October 1 for the December censors' examination. *(b)* At this time the district secretary shall verify the applicant's diploma and shall deliver the application form to the Secretary of the Society not later than March 10 or October 10 respectively. *(c)* An applicant nonresident in Massachusetts shall apply to the secretary of the Suffolk District Medical Society and shall be examined by the censors thereof. *(d)* Consideration of a late application shall be postponed until before the next succeeding examination. *(e)* The names of all such applicants, their addresses, medical schools, dates of graduation and the names and addresses of the various district secretaries shall be published in a list in the first number of the *New England Journal of Medicine* on or after April 1 or November 1. *(f)* Confidential communications regarding the qualifications of applicants for fellowship shall be requested of the fellows of the Society to be sent to the appropriate district secretary not later than April 15 or November 15.

(g) "An applicant for fellowship who is a graduate of a foreign medical school or a domestic medical school not on the list recognized by the Council or of a medical school no longer in existence, and who has practiced for a minimum of five years, shall apply for fellowship in like manner with the following exceptions and additions:

(h) "The application form must be submitted to the district secretary not later than February 15 or September 15. *(i)* At this time also the applicant must submit the name and address of a fellow of the Society who has agreed to act as his sponsor. *(j)* The sponsor's duty is to obtain from fellows of the Society who are acquainted with the applicant and his work, confidential written opinions regarding his qualifications for fellowship to be mailed directly to the district secretary not later than March 15 or October 15. *(k)* The application form of such an applicant shall be delivered by the district secretary to the Secretary of the Society not later than February 20 or September 20. *(l)* A list, similar to that of applicants who are graduates of recognized schools, but with the addition of names and addresses of sponsors shall be published in the first number of the *New England Journal of Medicine* on or after March 5 or October 5.

(m) "The president, secretary and supervising censor of the district society, sitting as a local board of membership, shall then gather such further information as is deemed necessary to determine whether an applicant is a capable and conscientious practitioner of medicine and possesses a good professional reputation among his colleagues. *(n)* Every candidate must be personally interviewed by this board.

(o) "The district secretary shall deliver to the chairman of the Committee on Medical Education a complete confidential file of all applications including correspondence, and the written recommendations of the local board with supporting reasons for advocating the acceptance or refusal of each applicant not later than April 1 or November 1. *(p)* The committee shall then determine whether or not each candidate shall be approved for examination by the censors, and shall notify the district secretary and each applicant of their decision not later than April 20 or November 20."

(a. Provisions unchanged except for dates. The system of definite unchanging dates from year to year is utilized throughout except in the case of examination dates, rather than the present method of dating by giving the number of weeks before the examination. The present method has always caused confusion in the minds of district secretaries and applicants alike since the actual date differs each year. Dates are set so as to allow ample time for the district secretaries, the secretary of the Society, the editor of the Journal, *the local boards of membership and the Committee on Medical Education to perform their duties prop-*

erly, as well as to allow no misunderstanding in anyone's mind concerning the date by which certain duties should be finished. Anyone who has not been one of the above mentioned officers has difficulty in appreciating the importance of this point.

b. *Transporting bulky framed diplomas to be shown to more than one official of the Society, as now occurs, is unnecessary. The Secretary of the Society has to verify and edit certain information on the application blanks before publication in the* Journal.

c. *Unchanged.*

d. *Nothing is more troublesome to all the officials concerned than attempting to handle late applications, which now are submitted up to the very eve of the examination and which are always coupled with requests for special consideration.*

e. *Unchanged except as to dates.*

f. *Occasionally unfavorable information of importance about an applicant exists. If it is withheld by an applicant's colleagues and an applicant is admitted to the Society, responsibility should rest on those who withheld the information. Such information when made available is always treated confidentially.*

g. *Unchanged in essentials.*

h. *The difference in dates from those in* a *is due to the more numerous procedures required in the cases of graduates of unapproved schools.*

i *and* j. *Sponsorship of an applicant who is a graduate of an unapproved school is a new proposal. Previously the applicant always personally approached his colleagues and asked for written recommendations. This system produced recommendations some of which were retracted by their writers in separate communications, and other recommendations which were obviously written by fellows who were only casually acquainted with the applicant, and others which were refuted by other available information. It is hoped that the new system will alleviate the embarrassment of an applicant's personally asking for a recommendation from a fellow who does not feel he can honestly give it.*

k. *See* b.

l. *Unchanged, except as to dates.*

m. *This change is the most fundamental of all those suggested. The Committee on Medical Education and Medical Diplomas has sensed for a long time how helpless it was in obtaining adequate information on which to determine the desirability of candidates for fellowship; this point has already been discussed more fully in the formal report. It is believed that a local board will be in every way better fitted to obtain this information than the central committee. The number of men on the board is small, they are already in positions of responsibility in their local society, and two of the three are already members of the board of censors, which eventually will examine those candidate finally approved. Further, it is very definitely felt that in the case of graduates of unrecognized schools the essential responsibility of whether or not they should be admitted to membership in the local society should lie with their own nearby colleagues, not with those farther afield. See Recommendation 11* e.

n. *Unchanged, except that the interview shall be carried out by the local board rather than the central committee.*

o *and* p. *This provides that the central committee shall take the responsibility of seeing that on one hand undue pressure has not been brought to bear on the local board to recommend for approval an undesirable applicant, nor on the other hand has unwarranted local prejudice barred from approval a desirable applicant.)*

10. *Chapter V, Section 3:* In line 4 on page 17 after the words, "applicants for fellowship;", insert the clause "they shall see that each applicant pays the examination fee;" *(See Recommendation 8* a. *This is inserted as it becomes a new duty for the district secretary.)*

11. *Chapter VII, Section 5:* First two paragraphs to be changed to read as follows:

(a) "The Committee on Medical Education shall consist of five fellows. It shall consider all matters relating to medical education which may be referred to it by the Council. *(b)* It shall review the case of every applicant for fellowship who presents according to the provisions of Chapter V, Section 2, a diploma from a medical school not on the list recognized by the Council. *(c)* It shall have the power to approve for examination by the censors such an applicant, and all decisions of the committee thereon shall be final. *(d)* It shall revise the list of medical schools recognized by the Council whenever it appears necessary."

(a. *Unchanged.*

b. *Changed in accordance with* 9 o *and* p.

c. *Unchanged.*

d. *Changed in that previously the committee had to await direction by the Council to accomplish this duty. It is believed that this list should conform to that of the medical schools approved by the American Medical Association, which is changed from time to time. The present list dated 1934 needs sixteen changes to bring it into such conformity.)*

A recent ruling by the President reversed the previous interpretation of the provisions of the by-laws regarding the application for readmission to the Society of a former fellow whose resignation had been requested by the Committee on Ethics and Discipline. Inasmuch as the individual in question was a graduate of an unrecognized school, it was ruled that he had to appear before the Committee on Medical Education and Medical Diplomas for approval, before being allowed to appear before the censors. Due to information requested from the chairman of the Committee on Ethics and Discipline, the Committee on Medical Education and Medical Diplomas disapproved the application. The latter committee, as a result of this case, believes that it should have no jurisdiction in such cases of readmission to the Society, and as a result studied the provisions of the by-laws regarding readmission. With the approval of the Committee on Ethics and Discipline and the Committee on Membership it recommends that the following changes be made in the by-laws:

12. *Chapter I, Section 7:* To read as follows: "The resignations of fellows whose assessments have been paid in full or remitted may, on recommendation of the Committee on Membership, be accepted by the Council and sent to the treasurer of the Society." *(The sentence deal-*

ing with readmission is deleted. The matter is now dealt with in Recommendation 14 a.*)*

13. *Chapter I, Section 8:* Omit last paragraph, "Fellows who have been deprived . . . secretary of the general Society." *(The sentences dealing with restoration to fellowship are deleted. The matter is now dealt with in Recommendations 14* a, b, c, d, *and* e.*)*

14. *Chapter I:* Add *Section 10,* to read as follows:

(a) "Former fellows who desire to be readmitted to the Society shall make application in writing addressed to the Council and sent to the secretary of the Society. *(b)* Such applications shall be referred for investigation and personal interview to the local boards of membership, which shall report their recommendations to the Committee on Membership. *(c)* The committee shall render the final decision as to whether to recommend to the Council the readmission of former fellows. *(d)* The Council shall have the power to readmit former fellows so recommended. *(e)* Boards having under consideration the applications of fellows whose resignations have been requested by the Committee on Ethics and Discipline, or who have been deprived of fellowship under the terms of section 8, clause *(c),* shall consult with the Committee on Ethics and Discipline before reporting their recommendations."

(a *and* b. *The distinction formerly made in Chapter I, Sections 7 and 8, between the method used in readmitting to fellowship those fellows who having "resigned" and those who having been "deprived of the privileges of fellowship" desire to rejoin the Society has been eliminated. It is believed that the local boards of membership can more adequately investigate the facts surrounding a fellow's separation from the Society and the altered situation that leads him to seek readmission than can either the censors or a specially appointed committee, as is the practice at the present.*

c. *The Committee on Membership should retain jurisdiction to review the recommendations of the local boards as it does at present in all cases of deprivation of fellowship. At the present it has no jurisdiction in cases of readmission to the Society following resignation.*

d. *The Council should have the full power of readmission of all former fellows recommended by the Committee on Membership. At present it has no jurisdiction in cases of readmission to the Society following resignation.*

e. *At present in cases where the Committee on Ethics and Discipline has requested a fellow's resignation as a form of discipline, and such resignation has been received, and the fellow later reapplies for readmission, the Committee on Ethics and Discipline has no jurisdiction in the matter of readmission. If the fellow in question is a graduate of an unrecognized school he must appear at present before the members of the Committee on Medical Education and Medical Diplomas, who if they approve his application pass him on to the censors for examination. This procedure is most illogical, since those who know nothing about the fellow deal with his readmission, while those who know everything about him have no official hand in the matter. At present the Council acting on separate reports of the Committee on Ethics and Discipline and of the Committee on Membership may deprive a fellow of the privileges of fellowship as provided in Chapter I, Section 8* (c). *With such a fellow desiring restoration to fellowship, a special committee is appointed to consider his case, and the by-laws provide that this committee must include at least one member of the Committee on Ethics and Discipline. The latter committee believes that with the institution of local boards of membership consultation with the Committee on Ethics and Discipline will provide sufficient opportunity for the board to know all the facts in the case before reporting its recommendations.)*

JOHN P. MONKS, *Chairman.*

* * *

For comparison, the by-laws referred to above are printed as they now stand:

CHAPTER I

FELLOWSHIP

Section 1. Applicants for admission to fellowship in the Massachusetts Medical Society are required to satisfy the censors that they are not less than twenty-one years of age; that they are of sound mind and of good moral character; that they possess a good English education; that their names and addresses and the name and address of the secretary of the district society in which they reside have been published in a special list in the *New England Journal of Medicine* at least two weeks prior to their examination by the censors; that they have received a diploma from a medical school or college recognized by the Council, or that they have, in each instance, received the approval of the Committee on Medical Education and Medical Diplomas; that they do not practice medicine in a manner contrary to the code of ethics of this Society; and they shall appear personally before the censors and satisfy them that the above requirements are fulfilled.

Section 6. Fellows shall be assessed annually such a sum as the Council may determine. The fiscal year shall begin on the first day of January. Assessments shall be payable in advance. The first assessment paid by a fellow admitted to the Society following the November examinations shall cover his dues for the succeeding fiscal year and shall be the amount fixed for that year.

Assessments may be remitted by the Council on recommendation by the Committee on Membership.

Whenever a fellow owing more than one annual assessment pays for one year or more, the payment or payments so made shall be considered as for the assessment or assessments longest due, and for no others.

Section 7. The resignations of fellows whose assessments have been paid in full, or remitted, may, on recommendation of the Committee on Membership, be accepted by the Council. Should such fellows apply for readmission, they shall appear personally before the censors, and the censors shall satisfy themselves that such applicants still meet the requirements of sections 1 and 2 of chapter I. Petitions to be allowed to resign should be addressed to the Council and sent to the Treasurer of the general Society.

Section 8. (a) Resident fellows who have neglected payment of three annual assessments, and who continue to neglect payment after notification by the Treasurer, shall be deprived of the privileges of fellowship, unless otherwise ordered, by the Council acting on a report of the Committee on Membership.

(b) Non-resident fellows who have neglected payment of two annual assessments, after removal from the state, shall be deprived of the privileges of fellowship in the same manner.

(c) Fellows who have been convicted in a court of law of a crime or misdemeanor involving moral turpitude or

who have been deprived of license to practice medicine in the Commonwealth, may be deprived of the privileges of fellowship by the Council acting on separate reports of the Committee on Ethics and Discipline and of the Committee on Membership, presented by the latter committee. Before a fellow shall be so recommended for deprivation, he shall have the privilege, if he requests it in writing, of a hearing by the joint committee.

Fellows who have been deprived of the privileges of fellowship and desire restoration shall make application in writing to the Council. Such application shall be referred to a committee for investigation and report. A committee having under consideration the application of a fellow deprived of the privileges of fellowship under the terms of clause *(c)* shall include in its membership at least one member of the Committee on Ethics and Discipline. All applications shall be addressed to the Council and sent to the Secretary of the general Society.

CHAPTER V

Censors and Supervisors

Section 1. The supervisors, representing the censors of the several district societies, shall constitute a board, which shall meet annually on the day appointed for the annual meeting of the Council. The board shall elect a chairman, who shall have power to call special meetings. Five supervisors shall constitute a quorum. The Secretary of the general Society shall act as secretary of the board. He shall call special meetings at the request of five supervisors. He shall keep a permanent record of the proceedings of the board, and shall provide, at the expense of the Society, papers and forms necessary for conducting examinations of applicants for fellowship. The board at its annual meeting shall adopt a uniform plan for the examination of applicants. The supervisors shall be paid the amount of their traveling expenses from the funds of the Society.

The supervisors shall be chairmen of their respective boards of censors, and shall cause the examinations of applicants to be conducted in strict conformity to the plan adopted by the Board of Supervisors.

Diplomas from medical schools and colleges no longer in existence, and diplomas from all foreign and domestic medical schools which are not on the list of medical schools and colleges recognized by the Council, shall be referred to the Committee on Medical Education and Medical Diplomas by the district secretary three weeks before an applicant shall be permitted to take an examination.

The censors of the several district societies shall meet semi-annually for the examination of applicants on the first Thursday in May and on the first Thursday in November. Special meetings may be held by order of the Council.

Section 2. An applicant for fellowship who is a graduate of a medical school or college recognized by the Council, shall apply, on a form furnished for the purpose to the secretary of the district in which he has a legal residence, at least six weeks before the date of a given examination. Applicants who are graduates from medical schools or colleges not upon the list recognized by the Council, shall apply not later than eight weeks before the time of a given examination. An applicant non-resident in Massachusetts shall apply to the secretary of the Suffolk District Medical Society, and shall be examined by the censors thereof. An applicant shall not be considered as possessing the requisite qualifications for fellowship unless approved by at least three censors.

Section 3. District secretaries, who shall act also as secretaries of their respective boards of censors, shall furnish applicants with forms adopted by the Board of Supervisors; they shall keep a complete record of all applicants for fellowship; they shall see that each successful applicant subscribes to the by-laws and code of ethics and pays within two weeks the dues for the current year; they shall furnish each new fellow with a copy of the digest, by-laws, code of ethics, and Medical Defense Act of the Society; and they shall present promptly after each examination, to the Treasurer of the general Society on a blank form furnished by him, a bill for censors' services together with a list of all the applicants examined. (See also chapter III, section 7.)

Following the examination of applicants, the district secretaries shall fill out, sign, and forward promptly to the Secretary of the general Society certificates stating that the successful applicants have complied with the requirements of the by-laws.

CHAPTER VII

Section 5. The Committee on Medical Education and Medical Diplomas shall consist of five fellows. It shall consider all matters relating to medical education which may be referred to it by the Council. When directed by the Council it shall revise the list of medical schools and colleges recognized by that body. Questions as to diplomas, referred to the censors under the provisions of chapter V, section 1, shall receive consideration and the decisions of the committee thereon shall be final.

It shall have power to recognize a medical diploma from a foreign medical school or college or from a domestic school or college not on the list recognized by the Council, when such a diploma is presented by an applicant who has practiced for a minimum of five years, offers proof to the committee that he is a capable and conscientious practitioner of medicine, and is recommended in confidential communications by a number of his colleagues who are fellows of the Society. The medical diploma and written recommendations of colleagues shall be sent by the district secretary to the chairman of the committee at least three weeks before any given examination. The committee shall interview personally all such applicants for fellowship.

It shall make a report to the annual meeting of the Council. On or before the fifteenth of January annually, it shall forward to the chairman of the Committee on Financial Planning and Budget an estimate of the expenses for the current year. All bills incurred shall be countersigned by the chairman and forwarded to the President for his approval.

COMMITTEE TO CONSIDER NEW OFFICERS AND BY-LAWS

Following the Council meeting of October 2, 1940, a committee was appointed by the president of the Massachusetts Medical Society to study the desirability of establishing the offices of president-elect and full-time or executive secretary and to suggest the necessary changes in the by-laws required to create these positions. At the Council meeting of February 5, 1941, the by-laws dealing with the creation of the office of president-elect

were accepted. At the same meeting the plan of having an executive secretary was accepted in principle, but the manner of electing the executive secretary was left to be determined.

At the Council meeting of October 2, 1940, a motion was made that this same committee should study the possibility of redistricting the Massachusetts Medical Society, with the idea of harmonizing its set-up with that of the American Medical Association and other state societies. The committee, in reporting at the Council meeting of February 5, 1941, took no action in respect to the problem of redistricting, but did suggest certain by-laws by which an executive committee of the Council could be established. In respect to the latter, the Council voted "that the committee continue and that it explore the possibilities of an executive committee so constituted that each district medical society would be represented."

Hence, your chairman has circularized the secretaries of the different district societies, asking them to secure, if possible, in the brief time between Council meetings, an opinion from their respective districts as to the best method of selecting an executive committee of the Council, and the possibility of redistricting the Massachusetts Medical Society.

In one way or another, your chairman has heard from six secretaries and from various sources has received the following impression: that no district desires a change in its boundaries and that a majority of the districts are opposed to such a change; that the idea of an executive committee of the Council is generally acceptable and that the districts prefer that each of them should be represented on this committee, no others to be made members of the committee except the officers of the Society. In accordance with this understanding, your committee, after consulting together, suggests the following changes in the by-laws.

JOHN HOMANS, *Chairman,*
JOHN FALLON,
PEIRCE H. LEAVITT,
FRANK R. OBER,
WALTER G. PHIPPEN, *ex officio,*
AUGUSTUS THORNDIKE, JR.

CHAPTER III

DISTRICT SOCIETIES

Section 5. (Additional)

The councilors of each district society shall meet immediately after the annual meeting of the district society in 1941 and elect one of their number to serve as a member of the Executive Committee of the Council in accordance with Chapter IV, Section 10. Thereafter, in a similar manner, they shall elect a new member from time to time.

Section 7. (Additional)

The secretary of each district society immediately after the annual meeting of the district society in 1941 shall call together its councilors for the purpose of electing a member of the Executive Committee of the Council and shall send the name of the member chosen to the Secretary of the general Society. He shall see that a new member is chosen in a similar manner to fill a vacancy as it occurs, in accordance with Chapter IV, Section 10.

CHAPTER IV

THE COUNCIL

Section 10. The Executive Committee shall consist of the President, President-Elect, Vice-President, Secretary and Treasurer *ex officiis*, and a councilor from each district medical society chosen in accordance with Chapter III, Section 5. The election of a councilor to the Executive Committee of the Council shall not be considered as leaving a vacancy among the councilors from the district he represents.

The councilors of each district society shall meet immediately after its annual meeting in 1941, as specified in Chapter III, Section 5, and in a similar manner at stated intervals as specified below, to choose one of their number to serve as a member of the Executive Committee of the Council.

A member of the Executive Committee shall serve for three years and shall not be eligible for re-election before the expiration of three years following the conclusion of his term of office; except that in 1941 six members shall be selected by lot to serve one year, six members shall be selected by lot to serve two years and six members shall be selected by lot to serve three years. Thereafter, six members shall be elected every year to succeed in office those whose terms are about to expire.

The Executive Committee shall meet at the call of the President at least once in each interval between Council meetings and may meet more often at the pleasure of the President. It shall assist the President in preparing for the consideration of the Council matters calling for action by the Council at its next meeting. It shall authorize action by the officers of the Society when circumstances require it, subject to the approval of the Council. It shall perform such other duties as the Council may require.

The consent of the Executive Committee shall be required to confirm the appointment, upon nomination by the President, of the Executive Secretary of the Society.

Upon request, members of the Executive Committee shall be paid the amount of their traveling expenses from the funds of the Society.

CHAPTER V

CENSORS AND SUPERVISORS

Section 1. The supervisors, representing the censors of the several district societies, shall constitute a board, which shall meet annually on the day appointed for the annual meeting of the Council. The board shall elect a chairman, who shall have power to call special meetings. Five supervisors shall constitute a quorum. The Secretary or Executive Secretary of the general Society shall act as secretary of the board. He shall call special meetings at the request of five supervisors. He shall keep a permanent record of the proceedings of the board, and shall provide, at the expense of the Society, papers and forms necessary for conducting examinations of applicants for fellowship. The board at its annual meeting shall adopt a uniform plan for the examination of applicants. The

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supervisors shall be paid the amount of their traveling expenses from the funds of the Society.

CHAPTER VI

Officers

Section 1. (Additional)

He shall call at least one meeting of the Executive Committee of the Council between Council meetings and may call more meetings if he so desires.

Section 4. The Secretary may assign to an Executive Secretary any or all the duties now to be enumerated, except as specified below:

The Secretary shall attend all meetings of the Society and of the Council, and shall record their respective proceedings in separate record books; and this duty he may not assign.

He shall cause to be engrossed and shall sign the diplomas of new fellows if satisfied that they have met the requirements of Sections 1 and 2 of Chapter I, and shall issue all diplomas and certificates of fellowship. He shall notify individual fellows, in appropriate instances, of votes by the Council granting permission, as the case may be, to retire, to resign, to change district membership, to have dues remitted, or of votes depriving them of the privileges of fellowship; and these duties he may not assign.

He shall act *ex officio* as secretary of all boards of trial; and this duty he may not assign.

He shall have custody of the seal of the Society and of all books, papers, manuscripts, prints and paintings belonging to the Society, except such as are in charge of the Treasurer; and this duty he may not assign.

He shall act *ex officio* as secretary of the Board of Supervisors and of the Committee on Publications and the Committee on Ethics and Discipline, and shall keep the records of each in a separate volume. He shall have custody of all records as thus kept.

He shall issue notices of the meetings of the Council. One month before the annual meeting of the Society, he shall issue to every fellow a program, which shall contain notification of the time and place of the annual meeting, notification of the stated meetings of the Council for the year and the meetings of the boards of censors, and information concerning the payment of assessments and the distribution of publications.

He shall record the Proceedings of the Council and of the Society. He shall keep a complete list of the fellows of the Society, with their addresses so far as known. He shall transfer fellows from one district to another under the terms of Chapter III, Section 2, and shall report to the Society at its annual meeting the changes in membership of the Society during the year.

He shall conduct the official correspondence of the Society, and shall notify officers, delegates and members of the committees of the general Society of their appointments and of their duties.

Under the direction of the Committee on Publications he shall issue at such intervals as may be determined by the Council a directory of officers and fellows of the Society, which shall be furnished upon request to fellows who are not in arrears.

He shall perform such other duties as the Society or the Council may require.

Section 5. An Executive Secretary shall be chosen by the Executive Committee of the Council upon nomination by the President. He shall hold office until his successor has been duly elected.

He shall perform such duties as are assigned to him in Section 4 of this chapter and by the Executive Committee. In general, he shall assist the officers of the Society and such standing and other committees as may request his services, and the Society shall have the first call upon his services.

He shall attend all meetings of the Council and, on request, attend the meetings of the Executive Committee of the Council, but shall not vote in either.

An Executive Secretary need not be a physician.

COMMITTEE ON STATE AND NATIONAL LEGISLATION

The following bills are scheduled for hearings at the State House during the week of March 31:

April 3

H. 1223 (Public Health). Petition of the Massachusetts Central Health Council and another for legislation to authorize the treatment of spastic paralysis at the Lakeville State Sanatorium. The committee believes that the Lakeville State Sanatorium is intended only for cases of nonpulmonary tuberculosis. *Opposed.*

H. 869 (Public Health). Petition of Enrico Cappucci and Lawrence P. McHugh for the suspension of the license of physicians who fail to make public their insurance company connections. This bill requires further investigation. *Undecided.*

H. 2007 (Public Health). Petition of Catherine E. Falvey for the establishment of a bureau for the care of inebriates under the Department of Public Health and relative to the powers and duties of such bureau. *Undecided.*

SECTION OF OBSTETRICS AND GYNECOLOGY*

Raymond S. Titus, M.D., *Secretary*
330 Dartmouth Street
Boston

Pernicious Vomiting in Pregnancy with Fatal Outcome

A thirty-three-year-old essential multipara in her fourth pregnancy was first seen when she was about ten weeks pregnant. She had been vomiting for two or three weeks before she consulted the doctor, and she was treated at home for two weeks before hospitalization.

The three previous pregnancies had resulted in a miscarriage at about eleven weeks, a spontaneous delivery at five months and a spontaneous delivery at six months. She had had no serious illness.

At the first examination the heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. The abdomen was negative except for a uterus that was enlarged to a size consistent with the period of amenorrhea. A blood Wassermann reaction was negative. The patient complained of vomiting of two to three weeks' duration.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

After a period of two weeks of inadequate medical treatment at home, the patient was sent to the hospital. On admission she was dehydrated. The tongue was dry and coated. The blood pressure was normal. The uterus was enlarged and in a normal anterior position.

For twelve days the patient was treated intensively with intravenous glucose, sedation and gastric feedings. On the thirteenth day after admission, she developed cerebral symptoms. On investigation by a consultant these were diagnosed as cerebral edema. The condition did not improve, and the patient died without operation on the twenty-fifth day after hospitalization.

Autopsy revealed a three months' pregnancy; nephrosis; acute venous congestion of the lungs and spleen with hemorrhage; edema of the brain, optic nerve and retinas; strangulation of the appendices epiploicae (torsion of pedicle); petechial hemorrhages in the epicardium and the mucosa of the stomach.

Comment. It is interesting in reviewing this history to note that the patient had three previous pregnancies but no living children. It is perfectly possible that the two pregnancies that ended spontaneously at five and six months respectively may have been induced by an underlying malnutrition. It is uncommon for patients exhibiting severe symptoms from vomiting in early pregnancy not to respond to intravenous glucose, sedation, gastric feedings and concentrated intramuscular injections of vitamin B. The unusual patient under this treatment continues to vomit and lose weight, shows increasingly rapid pulse and may develop jaundice. These symptoms demand medically that the uterus be emptied. Fortunately, therapeutic abortion for pernicious vomiting of pregnancy is extremely uncommon when the patients are treated adequately.

REFUND DISTRIBUTION

The Treasurer of the Massachusetts Medical Society makes the following report regarding the refund to district societies for 1941.

The Council voted to distribute the sum of $4000 to district societies. The total number of payments of annual dues received by the Treasurer by March 4, to be counted for the refund, was 4038. Therefore the refund to the district societies for each paid fellow is $0.99.

The following table gives the number of payments in, and the refund to, each district as of March 18:

District	Number Reported Paid	Refund
Barnstable	36	$36.12
Berkshire	109	107.91
Bristol North	65	64.83
Bristol South	158	156.42
Essex North	172	170.28
Essex South	242	239.58
Franklin	40	40.08
Hampden	299	296.01
Hampshire	50	49.98
Middlesex East	114	112.86
Middlesex North	103	101.97
Middlesex South	762	754.38
Norfolk	703	695.97
Norfolk South	120	118.80
Plymouth	117	115.83
Suffolk	521	515.79
Worcester	344	340.56
Worcester North	83	82.63
	4038	$4000.00

In 1940, for comparison, the total number of payments for the refund was 4058.

Charles S. Butler, M.D., *Treasurer.*

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning March 30:

BERKSHIRE

Thursday, April 3, at 4:30 p.m., in the Bishop Memorial Building, Pittsfield. Diagnosis, Treatment and Prognosis of Central-Nervous-System Syphilis. Instructor: Francis M. Thurmon. Harry G. Mellen, *Chairman.*

BRISTOL SOUTH (Fall River Section)

Tuesday, April 1, at 4:30 p.m., at the Union Hospital, Fall River. Acute Abdominal Pain: Its interpretation and management. Instructor: Richard B. Cattell. Howard P. Sawyer, *Chairman.*

FRANKLIN

Thursday, April 3, at 8:00 p.m., in the Library of the Franklin County Public Hospital, Greenfield. Recent Advances in Medical Therapeutics. Instructor: Charles L. Short. Halbert G. Stetson, *Chairman.*

HAMPDEN

Wednesday, April 2, at 4:00 p.m., at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, and at 8:00 p.m., in the Outpatient Department of the Skinner Clinic, Holyoke Hospital, Holyoke. Dermatitis and Eczema. Instructor: John G. Downing. Alfonso A. Palermo, *Chairman.*

HAMPSHIRE

Thursday, April 3, at 4:15 p.m., in the Nurses' Home of the Cooley Dickinson Hospital, Northampton. Pediatric Case Discussions. Instructor: James M. Baty. Robert C. Byrne, *Chairman.*

WORCESTER

Tuesday, April 1, at 8:30 p.m., in the Nurses' Home of the Milford Hospital, Milford. Therapeutic Uses of Preparations of Endocrine Glands: Thyroid gland, pituitary gland, ovary, testis and adrenal cortex. Instructor: William T. Salter. Joseph Ashkins, *Chairman.*

WORCESTER NORTH

Friday, April 4, at 4:30 p.m., in the Nurses' Home of the Burbank Hospital, Fitchburg. The Treatment of Varicose Veins. Instructor: E. Everett O'Neil. George P. Keaveny, *Chairman.*

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DEATH

MASON—Gilbert McC. Mason, M.D., of Dorchester, died March 17. He was in his seventieth year.

Born in Clinton, he attended Cushing Academy and received his degree from Boston University School of Medicine in 1898. From 1901 to 1910 he was demonstrator in anatomy at Boston University School of Medicine, and had also served on the staffs of the Carney and Forest Hills hospitals. Dr. Mason was a fellow of the Massachusetts Medical Society and the American Medical Association, as well as a member of the Association of Military Surgeons and the American Institute of Homeopathy.

His widow, a daughter, two brothers and two sisters survive him.

MISCELLANY

MAINE NEWS

Recently Registered Physicians

The following physicians were recently licensed to practice medicine in Maine:

Through Examination, July, 1940

Alton D. Blake, Jr., Waterville.
Aaron Bobrow, Hartford, Connecticut.
William E. Browne, Boston, Massachusetts.
Charles R. Geer, Portland.
Donald F. Larkin, Waterville.
Louis C. LeSieur, Biddeford.
Harry M. Lowd, Swampscott, Massachusetts.
Alexander D. Milligan, Hartford, Connecticut.
Leonard G. Miragliuolo, Providence, Rhode Island.
John F. Reynolds, Waterville.
Abraham E. Rosen, Bangor.
Mason Trowbridge, Upper Montclair, New Jersey.
Cecil H. Turner, Edmundston, New Brunswick.

Through Examination, November, 1940

Thomas J. Fritchey, Harrisburg, Pennsylvania.
Eugene G. Gormley, Houlton.
Karl V. Larson, Bangor.
Walter D. Mazzacane, New Haven, Connecticut.
John D. Prior, Hartford, Connecticut.
Ray A. Proctor, Boothbay Harbor.

Through Reciprocity

Harvey F. Doe, Trenton, New Jersey.
Charles L. Holt, Portland.
Edward F. Rohmer, Astoria, Long Island.
Deering G. Smith, Nashua, New Hampshire.
Victor L. Szanton, Deal Island, Maryland.
Robert A. Frost, Lewiston.
Donald Macomber, North Quincy, Massachusetts.
Ralf Martin, South Freeport.
Arthur P. Stebbins, Bangor.

New Association Members

The following physicians have been recently admitted to membership in the Maine Medical Association:

Paul V. Davis, Bridgton.
C. Lawrence Holt, Portland.
Kenneth E. Smith, Portland.
Victor L. Szanton, Bridgton.
Reynold A. E. Ulpts, Portland.
William W. Hardman, Togus.
Luverne Harris, Richmond.
Helen C. Provost, Augusta.
Chester W. Malmstead, Bangor.
Arthur P. Stebbins, Bangor.
Adelbert B. Allen, Corinna.
George C. Howard, Guilford.
John T. Guy, Elliot.

NOTES

Dr. Elliott P. Joslin was the speaker at the meeting of the Osler Clinical Society of the University of Vermont College of Medicine on Wednesday evening, March 12. The subject of Dr. Joslin's lecture was "The Application of Recent Physiological Studies to the Treatment of Diabetes Mellitus."

Harvard University recently announced the appointment of Dr. William C. Quinby as clinical professor of genitourinary surgery, emeritus, and Dr. Irving J. Walker as clinical professor of surgery, emeritus, on the faculty of Harvard Medical School to become effective September 1.

CORRESPONDENCE

MEDICAL CONTRACEPTIVE CARE

To the Editor: The public hearing on House 2035, the Massachusetts initiative petition for "an act to allow physicians to provide medical contraceptive care to married persons for the protection of life or health," will be held before the Committee on Public Health of the Legislature at 10:30 a.m., Thursday, April 3, in the Gardner Auditorium, State House, Boston.

The petition, which was initiated by ten prominent citizens of Massachusetts, including Drs. Nathaniel W. Faxon, of Newton, Frederick C. Irving, of Brookline, John C. Rock, of Boston, and Curtis C. Tripp, of New Bedford, was filed with 44,565 certified signatures of registered Massachusetts voters, more than double the 20,000 signatures required by law.

The petition is supported by the Committee for the Defense of Medical Rights, which reports that a majority of active members of the Massachusetts Medical Society have signed statements in support of the principle that physicians should be exempted from the restrictions of the present law.

Adoption by the Legislature of the proposed act would amend Chapter 272 of the General Laws by adding at the end of Section 21, the following:

> The provisions of this section and of section twenty which relate to the prevention of pregnancy and the prevention of conception shall not apply to treatment or prescription given to married persons for protection of life or health by or under the direction of physicians registered in accordance with the provisions of Chapter 112; nor to teaching in chartered medical schools; nor to publication or sale of medical treatises or journals.

Only Massachusetts and Connecticut have laws that have been enforced in such a way as to interfere with the right of a physician to prescribe contraceptives to a married woman for health reasons. Three states — North Carolina, South Carolina and Alabama — have incorporated postnatal contraceptive care into their maternal-health programs under the direction of their respective state medical societies.

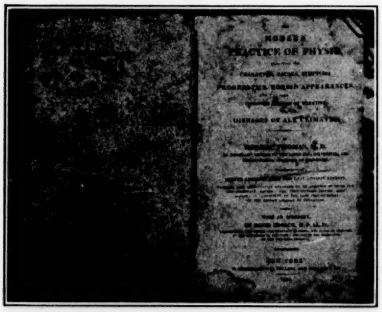
WILLIAM H. ROBEY, M.D., *President,*
Committee for the Defense of Medical Rights.

270 Commonwealth Avenue,
Boston.

DR. P. M. ARMSTRONG, OF HOOSICK, NEW YORK

To the Editor: A rather peculiar incident occurred to me recently. I was reading the June, 1939, issue of *Digest of Treatment* and noted a "Tombstone Inscription in Hoosick, N. Y." taken from the *New England Journal of Medicine.*

At first the name Dr. P. M. Armstrong did not register, but later I remembered that about fifteen years ago



a Mr. Armstrong gave me an old volume which had been his grandfather's and had been kept in the family for many years. This volume, *The Modern Practice of Physic,* by Robert Thomas, published in New York in 1825 by S. B. Collins, and Collins and Company, and marked number one volume from the library of P. M. Armstrong, of Hoosick, New York, evidently belonged to the person referred to in the inscription.

ARTHUR H. STOLL, M.D.

329 North Fifth Street,
Oxnard, California.

• • •

The tombstone inscription referred to above is as follows:

RUTH SPRAGUE.
dau. of Gibson
& Elizabeth Sprague,
died Jan. 11, 1846; aged
9 years 4 mo's & 3 days.

She was stolen from the grave
by Roderick R. Clow & dissected at Dr. P. M. Armstrong's office
in Hoosick N. Y. from which place
her mutilated remains were
obtained & deposited here.

Her body dissected by fiendish Men
Her bones anatomised,
Her soul we trust has risen to God,
Where few Physicians rise.

It was contained in a letter, "Body Snatching," submitted by Dr. Edward F. Timmins, of South Boston, and published in the March 16, 1939, issue of the *Journal.* ED.

RESTORATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held March 13, there was restored to Dr. Michael Litvich, 114 Shirley Avenue, Revere, Massachusetts, his license, which had been revoked on December 19, 1940.

STEPHEN RUSHMORE, M.D., *Secretary,*
Board of Registration in Medicine.

State House,
Boston.

REVOCATION OF LICENSE

To the Editor: The license of Dr. Claude G. Shepherd, formerly of 84 Humboldt Avenue, Roxbury, Massachusetts, was revoked by the Board of Registration in Medicine on March 13 because of violation of the law concerning narcotic drugs.

STEPHEN RUSHMORE, M.D., *Secretary,*
Board of Registration in Medicine.

State House,
Boston.

NOTICES

MEDICAL AND SURGICAL SUPPLY COMMITTEE

It will help England greatly in the care of victims of bombing raids and help England prepare for the coming invasion, if physicians in this country will give discarded or superfluous surgical instruments or surgical dressings.

Any such material should be sent to the Medical and Surgical Supply Committee, 420 Lexington Avenue, New York City.

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital amphitheater on Tuesday, April 8, at 8:15 p.m.

PROGRAM

Presentation of cases.

Disabilities in Reading and Their Remedying. Professor Walter F. Dearborn, Harvard University.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a. m.

MEDICAL CONFERENCE PROGRAM, APRIL

Tuesday, April 1 — Cell Respiration. Dr. W. Gleim.
Thursday, April 3 — Vitamin B Deficiency (motion picture film).
Friday, April 4 — Mental Changes in Paget's Disease. Dr. R. C. Wadsworth.
Tuesday, April 8 — Pancytopenia. Drs. William Dameshek and E. B. Miller.
Thursday, April 10 — The Problem of Vasomotor Rhinitis. Dr. L. R. Weiss.
Friday, April 11 — Certain Aspects in the Diagnosis and Treatment of Contagious Diseases. Dr. E. H. Place.
Tuesday, April 15 — Medical Ophthalmology. Dr. S. T. Clarke.
Thursday, April 17 — Endocrinological Relation between the Hypophysis and the Eye: Problems and facts. Dr. J. Igersheimer.
Friday, April 18 — What Happens to Alcoholics. Dr. Merrill Moore.
Tuesday, April 29 — Sir Charles Bell in Modern Dress. Dr. Leonard Carmichael.

Morning conferences will be suspended for the week of April 21, during the meetings of the American College of Physicians.

On Wednesday and Saturday mornings throughout the month, Dr. S. J. Thannhauser will give a medical clinic on hospital patients.

BOSTON SOCIETY OF BIOLOGISTS

There will be a meeting of the Boston Society of Biologists at the Harvard Medical School, Amphitheater E, on Wednesday, April 30, at 8 p.m.

PROGRAM

Chemical Conjugation of Antibodies without Destruction of Their Function. Dr. Albert H. Coons.
Production of a Condition Resembling Typhoid Fever by Means of a Purified Antigen of the Typhoid Bacillus. Mr. Herbert R. Morgan, A.M.
Results Obtained in a Laboratory Study of the Recent Epidemic of Influenza. Dr. John F. Enders.
The Production of Tetanus Toxin on a Peptone-Free Medium. Dr. J. Howard Mueller.

Dinner will be served in the main dining room of Vanderbilt Hall, Harvard Medical School, at 7 p.m. The rules of the dormitory do not permit the attendance of ladies at the dinner. Reservations should be made not later than Monday, April 28.

MASSACHUSETTS PUBLIC HEALTH ASSOCIATION

A business meeting of the Massachusetts Public Health Association will be held at the time of the New England Health Institute on Thursday, April 3, in Parlor A, Hotel Statler, Boston, at 1 p.m.

SALEM TUMOR CLINIC

A teaching clinic on chronic cystic mastitis, to be followed by the presentation of cases of breast disease, will be held at the Salem Hospital on Friday, April 25, at 9 a.m. The clinic will be conducted by Dr. Shields Warren.

Members of the Massachusetts Medical Society are cordially invited to attend.

WACHUSETT MEDICAL IMPROVEMENT SOCIETY

The next meeting of the Wachusett Medical Improvement Society will be held at the Holden District Hospital on Wednesday, April 2, at 6:30 p.m. Dr. Foster L. Vibber, of Worcester, will speak on "A Practical Application in Neurology and Psychiatry."

AMERICAN PUBLIC HEALTH ASSOCIATION

The seventieth annual meeting of the American Public Health Association will be held in Atlantic City, New Jersey, from October 14 to 17. The American School Health Association, the Association of Women in Public Health, the National Organization for Public Health Nursing, the International Society of Medical Health Officers, the New Jersey Health and Sanitary Association, the American Social Hygiene Association, the Conference of State Sanitary Engineers, the Conference of Municipal Public Health Engineers, the Conference of State and Provincial Public Health Laboratory Directors, the Conference of State Directors of Local Health Administration and the Conference of Pneumonia Control Officers will meet in conjunction with the association.

It will bring 4000 public-health workers to Atlantic City for a series of scientific meetings covering all phases of health protection and promotion. For further information, address the American Public Health Association, 1790 Broadway at 58th Street, New York City.

AMERICAN ACADEMY OF PHYSICAL MEDICINE

The nineteenth annual meeting and scientific session of the American Academy of Physical Medicine will be held in New York City, April 28, 29 and 30. The headquarters will be at the Hotel Pennsylvania, where lectures, symposiums, clinical papers, motion pictures and exhibits will be presented, with clinics at the Medical Center, New York Orthopaedic Hospital, Post Graduate Hospital and the Skin and Cancer Hospital. There will be an evening session at the Academy of Medicine and a banquet at the Hotel Pennsylvania.

The scientific program will be open to the medical profession without registration fee. For further information, write to Dr. Herman A. Osgood, Secretary, 144 Commonwealth Avenue, Boston.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, MARCH 30

MONDAY, MARCH 31

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, APRIL 1

*9–10 a.m. Cell Respiration. Dr. W. Gleim. Joseph H. Pratt Diagnostic Hospital.

12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

WEDNESDAY, APRIL 2

New England Health Institute. Hotel Statler, Boston.

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital.

THURSDAY, APRIL 3

New England Health Institute. Hotel Statler, Boston.

*9–10 a.m. Vitamin B Deficiency (motion picture film). Joseph H. Pratt Diagnostic Hospital.

1 p.m. Massachusetts Public Health Association, business meeting. Parlor A, Hotel Statler, Boston.

FRIDAY, APRIL 4

New England Health Institute. Hotel Statler, Boston.

*9–10 a.m. Mental Changes in Paget's Disease. Dr. R. C. Wadsworth. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, APRIL 5

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

MARCH 31–APRIL 4 — Sixth Annual Postgraduate Institute of the Philadelphia County Medical Society. Page 349, issue of February 20.

APRIL 1–29 — Joseph H. Pratt Diagnostic Hospital. Medical conference program. Page 579.

APRIL 2 — Wachusett Medical Improvement Society. Page 579.

APRIL 3 — Hermann M. Biggs Memorial Lecture. Page 531, issue of March 20.

APRIL 6 — Free public lecture, Quincy City Hospital. Page 436, issue of March 6.

APRIL 8 — Harvard Medical Society. Page 578.

APRIL 10 — New England Society of Psychiatry. Page 531, issue of March 20.

APRIL 10 — Pentucket Association of Physicians. Page 263, issue of August 15.

APRIL 21–25 — American College of Physicians. Page 1065, issue of June 20.

APRIL 25 — Salem Tumor Clinic. Page 579.

APRIL 28–30 — American Academy of Physical Medicine. Scientific session. Page 579.

APRIL 30 — Boston Society of Biologists. Page 579.

MAY 5–9 — American Association of Industrial Physicians and Surgeons and American Industrial Hygiene Association. Page 484, issue of March 13.

MAY 13–16 — National Gastroenterological Association. Hotel Commodore, New York City.

MAY 21, 22 — Massachusetts Medical Society, Boston.

MAY 28–JUNE 2 — American Board of Obstetrics and Gynecology. Page 262, issue of February 6.

MAY 30–JUNE 2 — American College of Chest Physicians. Hotel Statler, Cleveland, Ohio.

JUNE 2–6 — American Medical Association. Cleveland, Ohio.

OCTOBER 14–17 — American Public Health Association. Page 579.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

APRIL 2 — Pediatric Problems in General Practice. Dr. Joseph Garland. Addison Gilbert Hospital, Gloucester.

MAY 14 — Relation of the Doctor to the Law. Mr. Leland Powers. New Ocean House, Swampscott.

FRANKLIN

MAY 13 — This meeting will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

MAY 8 — Censors' meeting. Hotel Puritan.

SUFFOLK

APRIL 30 — Page 604, issue of October 10.

MAY 1 — Censors' meeting. Page 261, issue of February 6.

WORCESTER

APRIL 9 — Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOK REVIEWS

The Early Diagnosis of the Acute Abdomen. By Zachary Cope, A.B., M.D., M.S. (Lond.), F.R.C.S. (Eng.). Eighth edition. 8°, cloth, 257 pp., with 36 illustrations. London: Oxford University Press, 1940. $3.75.

This handy volume is essentially a diagnostic primer. Its value lies in its simplicity and proper emphasis of well-established facts rather than in any new analysis of symptoms or signs. The author stresses continually the need for accurate diagnosis in patients with acute abdominal symptoms. To accomplish this it is necessary to take a very careful history and to make a thorough physical examination. The urinary and blood findings are valuable supplementary data, although the author says little about the white-blood-cell count and nothing about the value of a differential count of the white blood cells.

In no other group of cases is judgment at a greater premium than in the diagnosis of acute surgical conditions of the abdomen. Such patients often enter in the early morning hours; they present the problem of pain that must be relieved; and on the basis of a few available facts one must decide whether operation is necessary and, if so, where the incision should be made. Cope has ably summarized the classic pictures, and has also indicated some of the leads that show the way when the picture is very confusing. The intangibles that cannot properly be put in writing and that must be interpreted can be mastered only through study of and experience with patients. Is spasm voluntary or involuntary? Are signs at the base of the right lung primary, or secondary to abdominal disease? Are the urinary findings due to a pelvic appendix? The answers to questions such as these rest entirely on judgment and experience.

To the medical students in this country and abroad this volume will be a great friend in guiding them through the intricacies and pitfalls of diagnosis in acute abdominal conditions. This new edition offers only slight changes from the previous ones.

Manual of Cardiology: Clinical methods and case histories as problems for study. By William Duncan Reid, A.B., M.D. 8°, cloth, 364 pp. London: Oxford University Press, 1940. $3.50.

The first one hundred and thirty-five pages of this book describe the clinical methods of the author. The rest of the book is concerned with a description of a series of fifty-six case histories followed in a separate section by discussions of the cases. The author admits that "the language of Section I is purposely very informal," but although this may serve his purpose of making "the text easier to read and more forceful," it creates an impression of carelessness. This is added to by the various errors in spelling and syntax, and the irritatingly poor proofreading. It seems unnecessary to mention the very unimportant signs of Duroziez and Graham Steell in a book of this sort, doubly so when the names are misspelled on each occasion.

Much of the discussion of clinical methods will be useful for the undergraduate student, and since the book is not intended as a textbook, it should not be too harshly judged by its omissions. Some rather obvious ones, however, may be noted, such as the failure to mention pulmonary infarct as the commonest cause of jaundice in cardiac patients, the inadequate description of the mechanism of gallop rhythm that is such an important physical sign, and the omissions of venesection in the treatment of acute pulmonary edema and of oxygen in acute coronary occlusion or cardiac failure.

The method of presentation by case histories of the material in Sections II and III has become established as a valuable technic. The case reports are, at times, instructive, but often one is asked to consider the diagnosis on the basis of inaccurate observations purposely given to indicate the errors of examination. It is questionable if this teaches anything except to mistrust all examinations save one's own. It is used by the author, for example, to illustrate errors in the diagnosis of the presystolic murmur that his colleagues seem so often to have found without anatomic basis. The discussion of this murmur is rather naïve in the light of present knowledge of the mechanism of heart sounds and murmurs.

The diagnosis of some of the cases may be questioned. For example, Case 28 is considered pulmonic stenosis and interventricular septal defect. In the absence of cyanosis or clubbed fingers, this seems unlikely. A septal defect alone is more probable.

The book will teach the beginner many practical points, and the case reports are a stimulus to diagnosis. The chief value of the book is in emphasizing methods of approach to cardiac problems, and it should be helpful mainly for undergraduate instruction.

Management of the Cardiac Patient. By William G. Leaman, Jr., M.D. 8°, cloth, 705 pp., with 255 original illustrations, two in color, 29 tables. Philadelphia: J. B. Lippincott Company, 1940. $6.50.

Progress in modern medicine is advancing at so rapid a pace that it is impossible for the general practitioner or internist to keep abreast of the entire current literature in even one field. The author of a good textbook is the reaper of this rich harvest; he must also select the wheat from the chaff. Dr. Leaman has succeeded in assembling in one volume most of the essential facts in the management of the cardiac patient. In the twenty-four chapters of this book are included most of the types of heart disease that are commonly met in the clinic and office. Since modern cardiology is dynamic rather than static, — that is, emphasis is laid on the etiology of the disease and the functional capacity of the patient, rather than on the description of the structural defect, — the author proceeds from that point of view. Each chapter has a theoretical exposition, just long enough to cover the essential facts, and short enough to hold the reader's interest. Variations that occur in the different types of heart disease are also considered. The book is up to date in that it includes most of the recent advances made in cardiology. There is a brief discussion of total ablation of the thyroid gland in selected cases of patients suffering from congestive cardiac failure or angina pectoris, proposed in 1933, as well as the latest Boston contribution — the Gross operation for the ligation of the arteriovenous communication in patent ductus arteriosus. Each chapter ends with a number of illustrative cases. The book contains numerous original illustrations, two of which are in color. These help to clarify a complicated subject. It is gratifying, indeed, that during these days of world chaos, this country is not only leading the world in scientific medical research, but also in making this knowledge available to many by textbooks as fine as this one.

Holt's Diseases of Infancy and Childhood: A textbook for the use of students and practitioners. By the late L. Emmett Holt, M.D., and John Howland, M.D. Revised by L. Emmett Holt, Jr., M.D., and Rustin McIntosh, M.D. Eleventh edition. 4°, cloth, 1421 pp., with 262 illustrations and 8 plates. New York: D. Appleton-Century Company, Incorporated, 1940. $10.00.

For many years Dr. Holt's book stood as the bible of pediatrics in the United States. Its status paralleled that of Osler's *Practice of Medicine;* every doctor knew it and almost every doctor owned it. With the passing of Dr. Holt and of Dr. Howland, who had collaborated with him, the distinctive personal touch naturally departed, but in the last analysis, the loss was largely sentimental. In the three successive editions for which the new authors are responsible, they have improved increasingly their auctorial abilities. Although the title page speaks of revision, more than revision has been done. They have emerged with a new book, a *Holt* much better, in certain respects, than the old one ever was.

It covers a great deal more ground. Originally, as the title implied, the book was almost wholly concerned with the child in sickness. Now, and to a greater extent in this edition than in its immediate predecessors, much space has been given to hygiene, nutrition, growth and feeding. But there is a still further departure in this latest issue. Because the general subject has so grown and because within the specialty new specialties have arisen, thirty-four subsidiary authors have been requisitioned for contributions. Such a move, we grant, is not always happy in its results; too often the disadvantages outweigh the benefits. A multiplicity of authors commonly means a multiplicity of points of view, an uneven scale of values and emphases. But teamwork has prevailed, and the unity of the book has not been appreciably disturbed. One might almost have anticipated which sections would require the greatest changes — those relating to diseases of the newborn, nutrition, allergy, endocrinology, the deficiency diseases, the diseases of the blood and some of the specific infections. These have been expanded, and although in previous editions the material at times has been compressed to keep the general bulk within bounds, this eleventh edition runs two hundred pages longer than the tenth. It should be added that there is an entirely new section on diseases of the eye; some of the pictures are different, and there are some new charts.

The more one studies this book, section by section, the more one is likely to be impressed. Apparently there are no significant omissions, and there is a gratifying sense of proportion and balance. If the facts are up to the minute, so too is the point of view. There are excellent bibliographies. The publisher has also done his part; in format, in printing and in clarity of illustration this book leaves little to be desired.

It may not be the old familiar *Holt;* it may not be indispensable. But it is nevertheless an outstanding book, one that can be trusted and valued and repeatedly used.

The Individual and his Society: The psychodynamics of primitive social organization. By Abram Kardiner, M.D. With a foreword and two ethnological reports by Ralph Linton. 8°, cloth, 503 pp. New York: Columbia University Press, 1939. $3.50.

Although this book will be of little interest to the general practitioner, it doubtless has value for the psychiatrist and psychoanalyst interested in reading on the periphery of their subjects. It also has a certain value for sociologists who are not impatient with such ultra-abstract attempts to co-ordinate anthropology, sociology, psychology and psychoanalysis.

Dr. Kardiner is a practicing psychiatrist. The material in this book is the product of a seminar held at the New York Psychoanalytic Institute over a period of three years. Although the main body of the material is anthropologic, eight primitive cultures having been studied in the seminar, the author seems to be concerned mainly with personality, and with a somewhat new and original methodology. There is here a kind of dialectic between basic personality structure and institutions.

The interrelations between personality and culture have been a subject of renewed interest among sociologists in recent years. This mature discussion of the subject should stimulate thought among those working on "the firing line" of this special field.

Dynamics of Inflammation: An inquiry into the mechanism of infectious processes. By Valy Menkin, M.D. 8°, cloth, 244 pp., with 50 illustrations and 27 tables. New York: Macmillan Company, 1940. $4.50.

This is a careful and well-documented report of the author's views and experimental work in the field of inflammation, particularly emphasizing the humoral aspects. His extensive researches in the field of leukotaxine and other substances are clearly presented.

After a brief historical survey, sections are devoted to the mechanism of capillary filtration, the capillaries in inflammation, the mechanism of increased capillary permeability, the migration of leukocytes into inflamed tissue, cellular sequence in inflammation, the phagocytic theory, the mechanism of leukocytosis with inflammation, inflammation in relation to immunity, the concept of fixation, the localization of foreign material in areas of inflammation, allergic and anaphylactic inflammation, the role of lymphatics in inflammation and inflammation and bacterial invasiveness in relation to resistance. There is an excellent bibliography.

The author's viewpoint can be summarized briefly as follows: the principal sequences in the development of inflammation are increased passage of fluid through the walls of the capillaries, localization of irritant and migration of the leukocytes.

Cancer: A manual for practitioners. The Committee on Publication: George W. Holmes, M.D., chairman, Shields Warren, M.D., and Ernest M. Daland, M.D. Editor: Channing C. Simmons, M.D. 8°, cloth, 284 pp. Boston: Rumford Press, 1940. $2.00.

This volume aims to assist the practitioner in the diagnosis of cancer at an early stage, while it is still amenable to treatment—a most commendable purpose. Compiled as part of the program for the control of cancer in Massachusetts, it has been sent to all the practitioners in this state.

The work is comprised of individual essays by men with wide clinical experience and a lively interest in the problems discussed. Most of the authors are Massachusetts men, and it is through their excellent work that the death rate from cancer in this state has finally shown some improvement.

If each practitioner sees only an occasional case of cancer during the year, he needs some work such as this to keep his suspicions of the disease alive. From this standpoint all the facts presented are useful. The only possible criticism is the arrangement of the chapters. It might have helped to develop and sustain the interest of busy practitioners if the first chapters had been practical rather than devoted to the historical and investigative aspects of cancer.

The Foot and Ankle: Their injuries, diseases, deformities and disabilities. By Philip Lewin, M.D. 8°, cloth, 620 pp., with 303 illustrations. Philadelphia: Lea and Febiger, 1940. $9.00.

This is a very complete and exhaustive review of all conditions concerning the foot and ankle. The illustrations, which are numerous and some of which are from other authors, make the text easy to understand.

The first part of the book takes up in detail the office or ambulatory treatment of various conditions, such as with shoes, supports and plaster casts. Then follow in detail the various operative procedures that are used in this country, with due credit to the originators. Dr. Lewin has kept a very good balance between operative orthopedics and other conditions, so that this book is of value to practitioners as well as to orthopedic surgeons.

Report on the Sex Question by The Swedish Population Commission. Medical Aspects of Human Fertility Series Issued by the National Committee on Maternal Health, Incorporated. Stockholm, 1936. Statens Offentliga Utredningar 1936:59. Translated and edited by Virginia Clay Hamilton, M.D. 8°, cloth, 182 pp., with 9 tables. Baltimore: Williams and Wilkins Company, 1940. $2.00.

Although this book touches on several angles of the sex question, it is mainly an argument for a liberalization of the laws in Sweden concerning the dissemination of birth-control information. It is a scientific treatise devoid of emotional bias. Considerable emphasis is placed on the decline of natality in Sweden, and there is an extensive discussion of probable causes. There is a warning against the intensive use of contraception to a point where it would endanger folk stock. This tendency to such intensive use is recognized by the commission, but the members believe that this would be more than offset if sociologic and economic conditions preventing early marriage were so adjusted as to eliminate this handicap. There is a very sane and dispassionate evaluation of the use of contraception in extramarital relations. There is an excellent chapter entitled "Sex Enlightenment: Its organization in a broadened and improved education for parenthood."

The Doctor and His Patients: The American domestic scene as viewed by the family doctor. By Arthur E. Hertzler, M.D. 8°, cloth, 316 pp. New York: Harper and Brothers, 1940. $2.75.

Dr. Hertzler's success with his previous volume, *The Horse and Buggy Doctor,* has led him to write a second book, not nearly so satisfactory as the first. To be sure, his object is somewhat different, for he is not telling the story of his life in this volume, but is attempting to analyze the lives of his patients. The comments are, in general, excellent, but there is also considerable uncertain thinking on problems that, although interesting, are not elucidated by the doctor's writing. There is perhaps not much to criticize in this book, but on the other hand, there is little to praise.

A Manual of the Common Contagious Diseases. By Philip Moen Stimson, M.D. Third edition, thoroughly revised. 12°, cloth, 465 pp., with 54 engravings and 6 plates, 4 in color. Philadelphia: Lea and Febiger, 1940. $4.00.

This reliable, up-to-date, pocket-sized manual is stripped of all nonessentials. The first two chapters deal with the general subject of infection, immunity and serum reactions. The last is concerned with the general management of contagious disease in hospital and home. The rest is devoted to the several specific diseases most commonly encountered in children—diphtheria, Vincent's angina, scarlet fever, measles, rubella, pertussis, mumps, varicella, smallpox, meningococcal meningitis and poliomyelitis. The manual discusses the etiology, pathology, diagnosis, complications, treatment and prevention of each disease. The printing and illustrations are excellent. There is a good index, and a helpful glossary. The book can be highly recommended to the student of medicine or of public health and the practitioner who wants to brush up on the latest accepted opinions in this field.